

Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	Jun 03	New e-mail delivery for search results now available
NEWS	4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	7	Sep 03	JAPIO has been reloaded and enhanced
NEWS	8	Sep 16	Experimental properties added to the REGISTRY file
NEWS	9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	11	Oct 24	BEILSTEIN adds new search fields
NEWS	12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	13	Nov 18	DKILIT has been renamed APOLLIT
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NEWS	15	Dec 04	CSA files on STN
NEWS	16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	17	Dec 17	TOXCENTER enhanced with additional content
NEWS	18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
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NEWS	22	Feb 24	PCTGEN now available on STN
NEWS	23	Feb 24	TEMA now available on STN
NEWS	24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	25	Feb 26	PCTFULL now contains images
NEWS	26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
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NEWS	28	Mar 24	PATDPAFULL now available on STN
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NEWS	30	Apr 11	Display formats in DGENE enhanced
NEWS	31	Apr 14	MEDLINE Reload
NEWS	32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS	34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
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NEWS	36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	38	May 15	Supporter information for ENCOMPAT and ENCOMPLIT updated
NEWS	39	May 16	CHEMREACT will be removed from STN
NEWS	40	May 19	Simultaneous left and right truncation added to WSCA

NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 43 Jun 06 PASCAL enhanced with additional data
NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:06:37 ON 01 JUL 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:06:42 ON 01 JUL 2003

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

DICTIONARY FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s 220488-46-OP/RN

L1 0 220488-46-OP/RN

=> d l1

L1 HAS NO ANSWERS

L1 0 SEA FILE=REGISTRY PLU=ON 220488-46-OP/RN

=> s l1

L2 0 220488-46-OP/RN

=> d 220488-46-OP/RN

'220488-46-OP' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'

The saved name for a query (or structure or screen set) must end with '/Q'. The saved name for an answer set must end with '/A'. The saved name for an L# list must end with '/L'. SDI request names must end with '/S'. To see a list of all saved query, answer set,, and L# list names for this loginid, enter "DISPLAY SAVED" at an arrow prompt (=>). Enter "DISPLAY SAVED/S" to see a list of SDI request names. Enter "DISPLAY SAVED/B" to see a list of BATCH search requests.

=> d 220488-46-OP/RN/Q

'220488-46-OP' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'

The saved name for a query (or structure or screen set) must end with '/Q'. The saved name for an answer set must end with '/A'. The saved name for an L# list must end with '/L'. SDI request names must end with '/S'. To see a list of all saved query, answer set,, and L# list names for this loginid, enter "DISPLAY SAVED" at an arrow prompt (=>). Enter "DISPLAY SAVED/S" to see a list of SDI request names. Enter "DISPLAY SAVED/B" to see a list of BATCH search requests.

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

2.40

2.61

FILE 'CAPLUS' ENTERED AT 14:10:21 ON 01 JUL 2003

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FILE COVERS 1907 - 1 Jul 2003 VOL 139 ISS 1

FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 130:168387?DN

'?' TRUNCATION SYMBOL NOT VALID WITHIN '168387?DN'

The truncation symbol ? may be used only at the end of a search term. To specify a variable character within a word use '!', e.g., 'wom!n' to search for both 'woman' and 'women'. Enter "HELP TRUNCATION" at an arrow prompt (=>) for more information.

=> s 130:168387/DN

L3 1 130:168387/DN

=> d l3 fbib hitstr abs total

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1999:113656 CAPLUS

DN 130:168387

TI Irreversible inhibitors of tyrosine kinases

IN Bridges, Alexander James

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9906378	A1	19990211	WO 1998-US15784	19980729
	W:	AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
				US 1997-54060P P	19970729
	AU 9887607	A1	19990222	AU 1998-87607	19980729
				US 1997-54060P P	19970729
				WO 1998-US15784W	19980729
	US 6127374	A	20001003	US 1999-269545	19990325
				US 1997-54060P P	19970729
				WO 1998-US15784W	19980729
	US 6562818	B1	20030513	US 2000-593031	20000613
				US 1997-54060P P	19970729
				WO 1998-US15784W	19980729
				US 1999-269545 A3	19990325
OS	MARPAT 130:168387				
AB	Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH2OH was treated with 4-FC6H4NO2 to give 4-PhCH2OC6H4NO2, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzoyloxyanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzoyloxyanilino)quinazolin-6-yl]acrylamide (I). I had an IC50 for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.				
RE.CNT	9	THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD			
		ALL CITATIONS AVAILABLE IN THE RE FORMAT			

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

6.22

8.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-0.65

-0.65

STN INTERNATIONAL LOGOFF AT 14:13:38 ON 01 JUL 2003

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS
 AN 1994:217715 CAPLUS
 DN 120:217715
 TI Quinazoline tyrosine Kinase-inhibiting anticancer agents
 IN Barker, Andrew J.
 PA Zeneca Ltd., UK
 SO Can. Pat. Appl., 99 pp.
 CODEN: CPXXEB
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2086968	AA	19930721	CA 1993-2086968	19930108
	CA 2086968	C	19980623		
				GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626
				GB 1992-23735	A 19921112
	ZA 9300015	A	19930720	ZA 1993-15	19930104
				GB 1992-1095	A 19920120
	AU 9331010	A1	19930722	AU 1993-31010	19930104
	AU 661533	B2	19950727		
				GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626
				GB 1992-23735	A 19921112
				HU 1993-94	19930115
	HU 63153	A2	19930728	GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626

Patel

<7/1/2003>

Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	23	Feb 24	TEMA now available on STN
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NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
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NEWS 43 Jun 06 PASCAL enhanced with additional data
NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:38:38 ON 01 JUL 2003

=> file reg

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:38:47 ON 01 JUL 2003

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STRUCTURE FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

DICTIONARY FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STN Note 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 10016280.5

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 14:39:14 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 302 TO ITERATE

100.0% PROCESSED 302 ITERATIONS

7 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 4998 TO 7082

PROJECTED ANSWERS: 7 TO 298

L2 7 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 14:39:21 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 6071 TO ITERATE

100.0% PROCESSED 6071 ITERATIONS

82 ANSWERS

SEARCH TIME: 00.00.01

L3 82 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 14:39:27 ON 01 JUL 2003

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FILE COVERS 1907 - 1 Jul 2003 VOL 139 ISS 1

FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L4 24 L3

=> d 14 fbib hitstr abs total

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:951575 CAPLUS

DN 138:117246

TI Mapping the Binding Site of a Large Set of Quinazoline Type EGF-R Inhibitors Using Molecular Field Analyses and Molecular Docking Studies

AU Hou, Tingjun; Zhu, Lili; Chen, Lirong; Xu, Xiaojie

CS College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China

SO Journal of Chemical Information and Computer Sciences (2003), 43(1), 273-287

CODEN: JCISD8; ISSN: 0095-2338

PB American Chemical Society

DT Journal

LA English

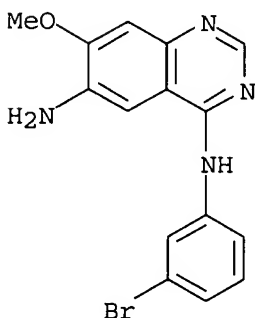
IT 171745-06-5

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(QSAR (quant. structure-activity relationship) studies on quinazoline type epidermal growth factor receptors (EGF-R) inhibitors using mol. field analyses and mol. docking studies)

RN 171745-06-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB In the current work, three-dimensional QSAR studies for one large set of quinazoline type epidermal growth factor receptor (EGF-R) inhibitors were conducted using two types of mol. field anal. techniques: comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA). These compds. belonging to six different structural classes were randomly divided into a training set of 122 compds. and a test set of 13 compds. The statistical results showed that the 3D-QSAR models derived from CoMFA were superior to those generated from CoMSIA. The most optimal CoMFA model after region focusing bears significant cross-validated r^2_{cv} of 0.60 and conventional r^2 of 0.92. The predictive power of the best

CoMFA model was further validated by the accurate estn. to these compds. in the external test set, and the mean agreement of exptl. and predicted log(IC50) values of the inhibitors is 0.6 log unit. Sep. CoMFA models were conducted to evaluate the influence of different partial charges (Gasteiger-Marsili, Gasteiger-Huckel, MMFF94, ESP-AM1, and MPA-AM1) on the statistical quality of the models. The resulting CoMFA field map provides information on the geometry of the binding site cavity and the relative wts. of various properties in different site pockets for each of the substrates considered. Moreover, in the current work, we applied MD simulations combined with MM/PBSA (Mol. mechanics/Possion-Boltzmann Surface Area) to det. the correct binding mode of the best inhibitor for which no ligand-protein crystal structure was present. To proceed, we define the following procedure: three hundred picosecond mol. dynamics simulations were first performed for the four binding modes suggested by DOCK 4.0 and manual docking, and then MM/PBSA was carried out for the collected snapshots. The most favorable binding mode identified by MM/PBSA has a binding free energy about 10 kcal/mol more favorable than the second best one. The most favorable binding mode identified by MM/PBSA can give satisfactory explanation of the SAR data of the studied mols. and is in good agreement with the contour maps of CoMFA. The most favorable binding mode suggests that with the quinazoline-based inhibitor, the N3 atom is hydrogen-bonded to a water mol. which, in turn, interacts with Thr 766, not Thr 830 as proposed by Wissner et al. (J. Med. Chem. 2000, 43, 3244). The predicted complex structure of quinazoline type inhibitor with EGF-R as well as the pharmacophore mapping from CoMFA can interpret the structure activities of the inhibitors well and afford us important information for structure-based drug design.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:487536 CAPLUS

DN 137:63250

TI Quinazoline derivatives as inhibitors of human EFG tyrosine kinase

IN Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002050043	A1	20020627	WO 2001-EP14569	20011212
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10063435	A1	20020704	DE 2000-10063435A	20001220
	AU 2002019174	A5	20020701	DE 2000-10063435	20001220
				AU 2002-19174	20011212
				DE 2000-10063435A	20001220

US 2002173509 A1 20021121

WO 2001-EP14569W 20011212
US 2001-23099 20011217
DE 2000-10063435A 20001220
US 2000-259201PP 20001228

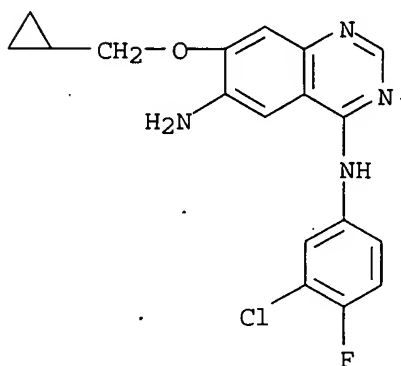
OS MARPAT 137:63250

IT **290304-07-3**

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 290304-07-3 CAPLUS

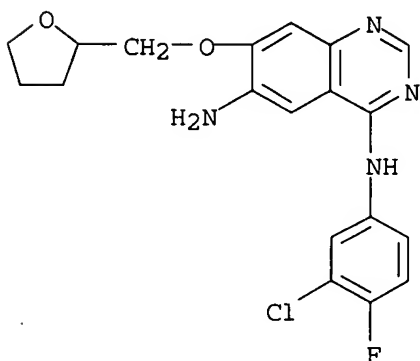
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy) - (9CI) (CA INDEX NAME)

IT **314771-75-0P 314771-76-1P 314771-77-2P****402855-03-2P 402855-04-3P 402855-05-4P****439081-58-0P 439081-59-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 314771-75-0 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2-furanyl)methoxy] - (9CI) (CA INDEX NAME)

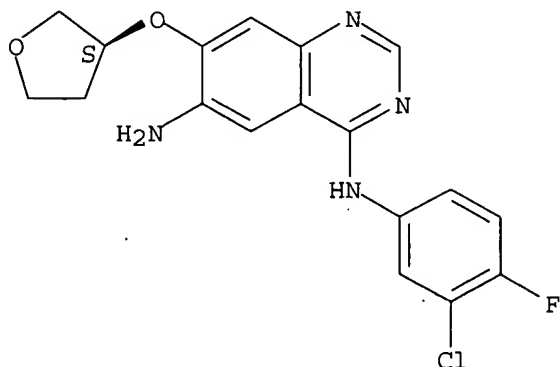


RN 314771-76-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-

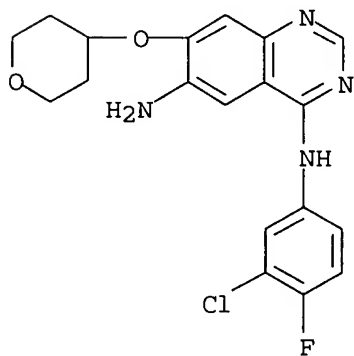
furanyl]oxy] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 314771-77-2 CAPLUS

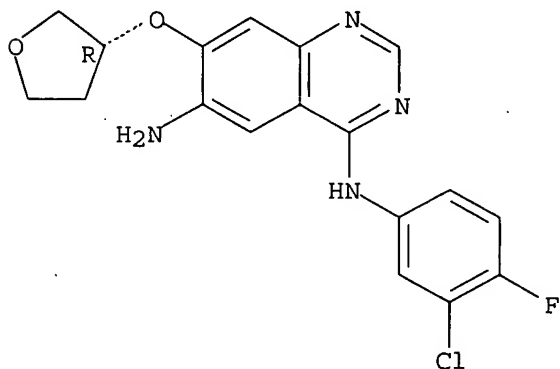
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)oxy] - (9CI) (CA INDEX NAME)



RN 402855-03-2 CAPLUS

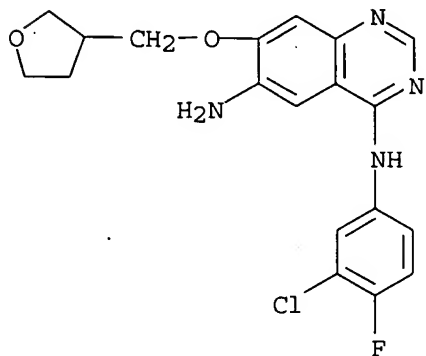
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3R)-tetrahydro-3-furanyl]oxy] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



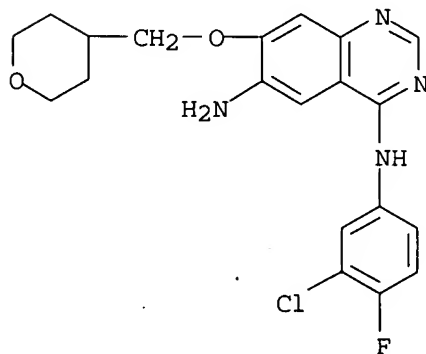
RN 402855-04-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-3-furanyl)methoxy] - (9CI) (CA INDEX NAME)



RN 402855-05-4 CAPLUS

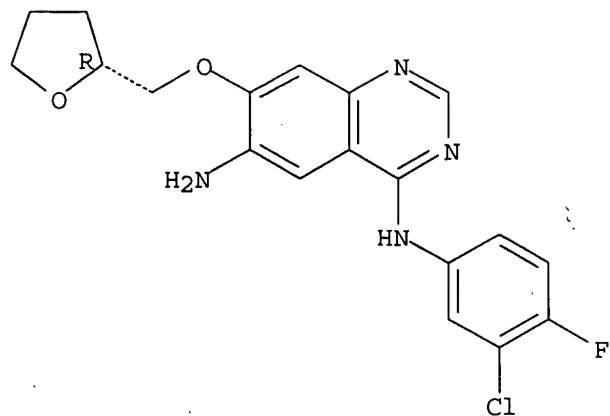
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)methoxy] - (9CI) (CA INDEX NAME)



RN 439081-58-0 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(2R)-tetrahydro-2-furanyl]methoxy] - (9CI) (CA INDEX NAME)

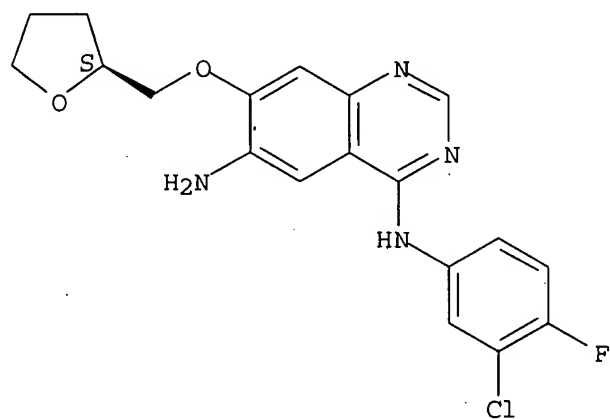
Absolute stereochemistry.



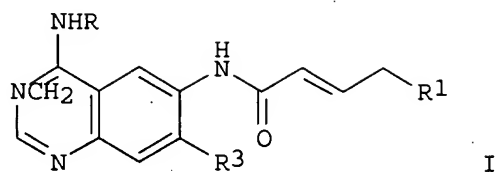
RN 439081-59-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(2S)-tetrahydro-2-furanyl]methoxy] - (9CI) (CA INDEX NAME)

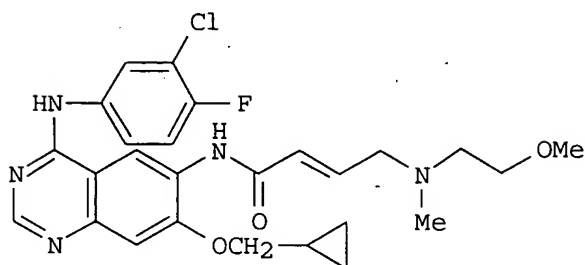
Absolute stereochemistry.



GI



I



II

AB Quinazoline derivs. I [R = PhCH₂, PhCHMe, 3,4-Cl(F)C₆H₃; R₁ = NMe₂, NEt₂, NEtCH₂CH₂OMe, N(CH₂CH₂OMe)₂, morpholino; R₂ = Me, Et, CHMe₂, cyclopropyl, CH₂CH₂OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R₃ = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranyloxy, 2-tetrahydrofuranylmethoxy, 3-tetrahydrofuranylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepd. for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepd. by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH₂CH₂OMe. II had an IC₅₀ against human EFG receptor kinase of 0.7 nM.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:171892 CAPLUS

DN 136:216762

TI Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

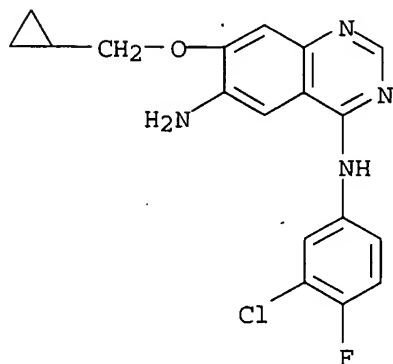
DT Patent

LA German

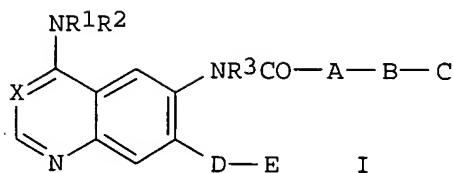
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018376	A1	20020307	WO 2001-EP9536	20010818
	W:				
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 2000-10042062A 20000826
DE 10042062 A1 20020307 DE 2000-10042062 20000826
AU 2001095482 A5 20020313 AU 2001-95482 20010818
DE 2000-10042062A 20000826
WO 2001-EP9536 W 20010818
EP 1315720 A1 20030604 EP 2001-976108 20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
DE 2000-10042062A 20000826
WO 2001-EP9536 W 20010818
US 2002115675 A1 20020822 US 2001-934631 20010822
DE 2000-10042062A 20000826
US 2000-230542PP 20000905
OS MARPAT 136:216762
IT **290304-07-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal
growth factor receptor signal transduction inhibitors)
RN 290304-07-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-
(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 =

Patel

<7/1/2003>

(substituted) Ph, PhCH₂, 1-phenylethyl; R₃ = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and MeSO₂OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:171891 CAPLUS

DN 136:216761

TI Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018375	A1	20020307	WO 2001-EP9534	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2002010444	A5	20020313	DE 2000-10042064	20000826
			AU 2002-10444	20010818
			DE 2000-10042064A	20000826
			WO 2001-EP9534 W	20010818
US 6403580	B1	20020611	US 2001-935498	20010823
			DE 2000-10042064A	20000826
			US 2000-230541PP	20000905

OS MARPAT 136:216761

IT 402723-54-0P 402723-56-2P 402723-58-4P

402723-60-8P 402723-61-9P 402723-62-0P

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402723-95-9P 402723-96-0P 402723-97-1P

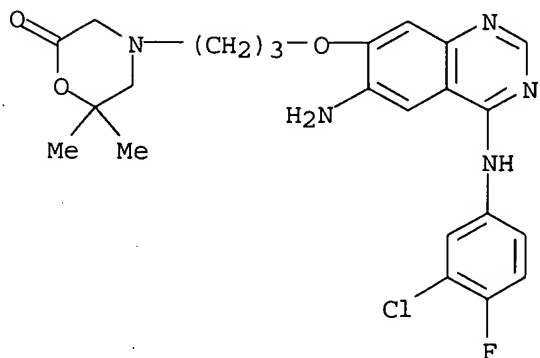
402723-98-2P 402723-99-3P 402724-00-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

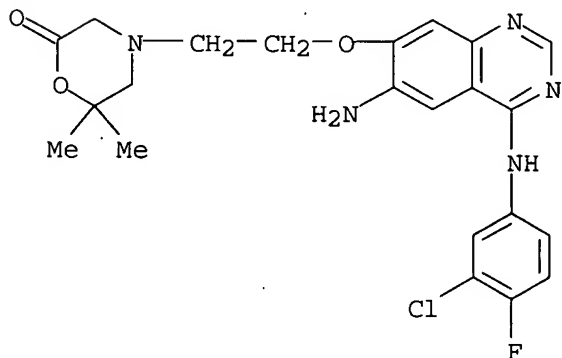
RN 402723-54-0 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-56-2 CAPLUS

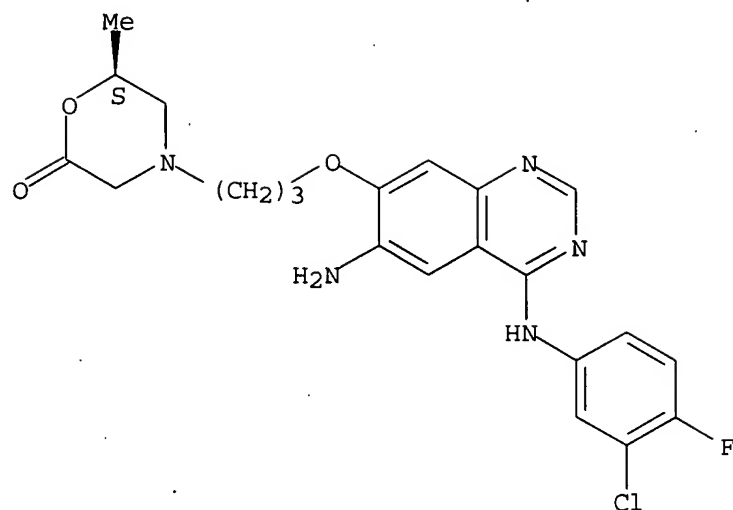
CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-58-4 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

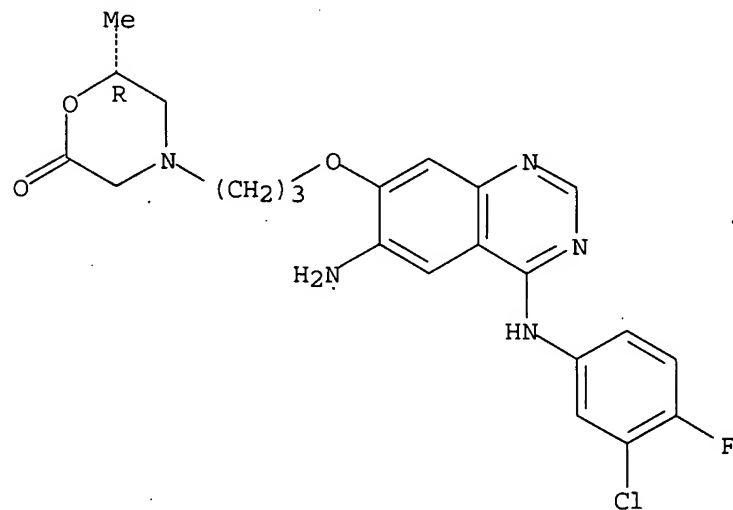
Absolute stereochemistry.



RN 402723-60-8 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

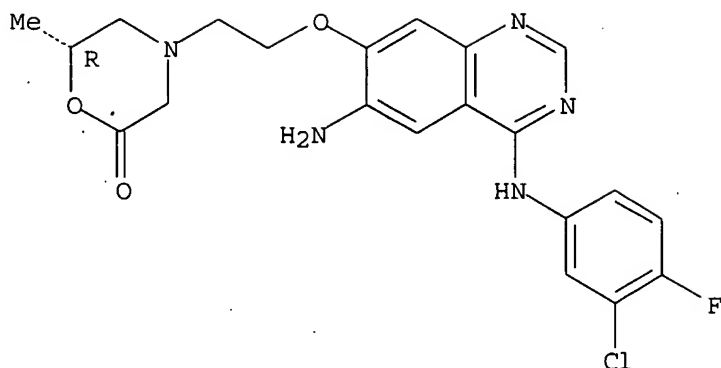
Absolute stereochemistry.



RN 402723-61-9 CAPLUS

CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

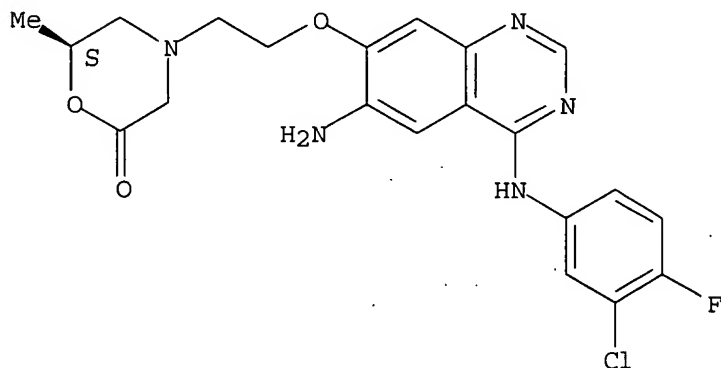
Absolute stereochemistry.



RN 402723-62-0 CAPLUS

CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

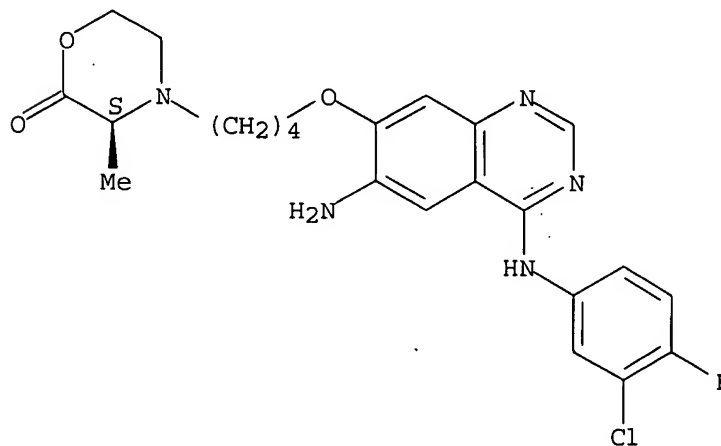
Absolute stereochemistry.

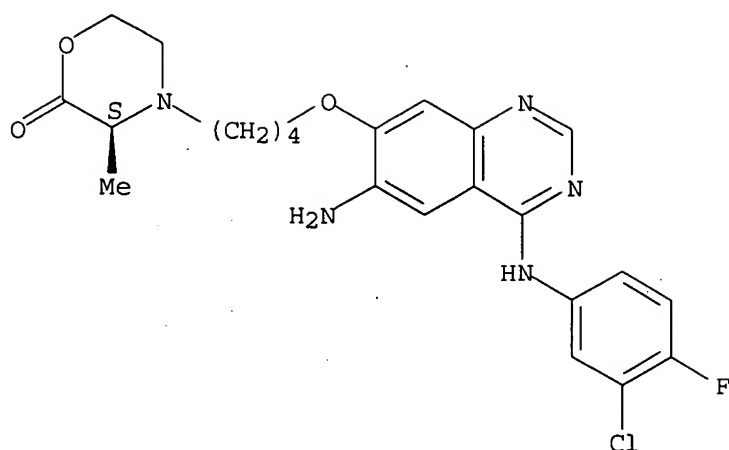


RN 402723-63-1 CAPLUS

CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-3-methyl-, (3S)- (9CI) (CA INDEX NAME)

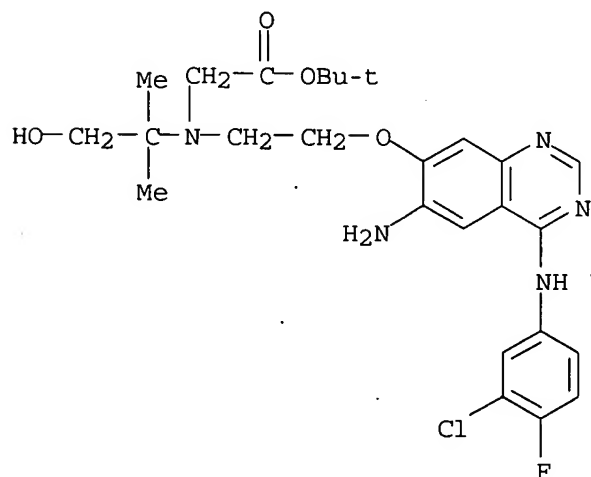
Absolute stereochemistry.





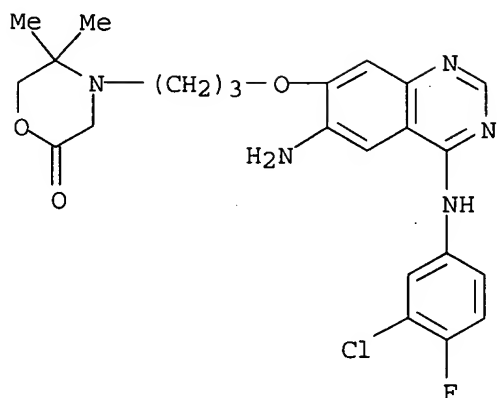
RN 402723-64-2 CAPLUS

CN Glycine, N-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-N-(2-hydroxy-1,1-dimethylethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



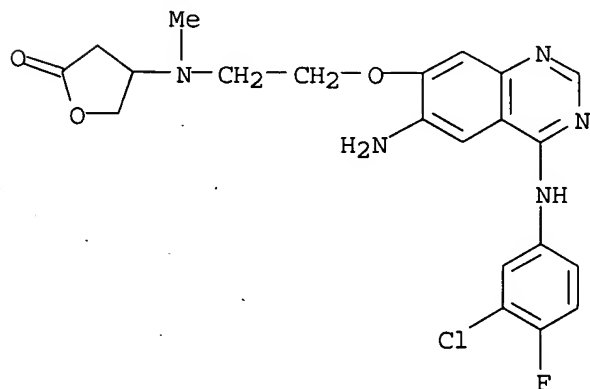
RN 402723-94-8 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



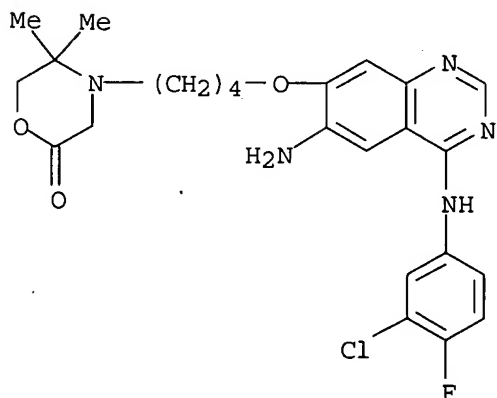
RN 402723-95-9 CAPLUS

CN 2(3H)-Furanone, 4-[[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]methyamino]dihydro- (9CI) (CA INDEX NAME)



RN 402723-96-0 CAPLUS

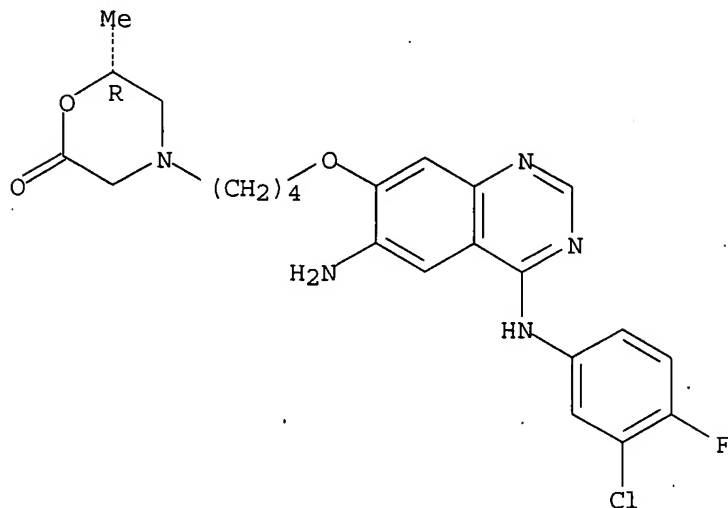
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-97-1 CAPLUS

CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

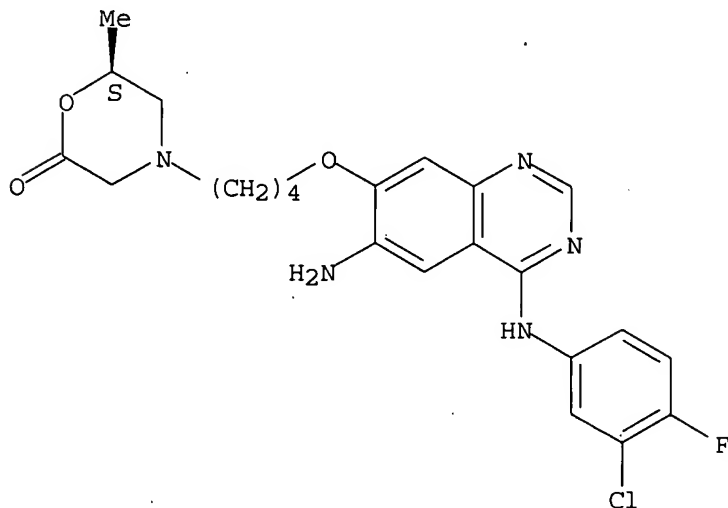
Absolute stereochemistry.



RN 402723-98-2 CAPLUS

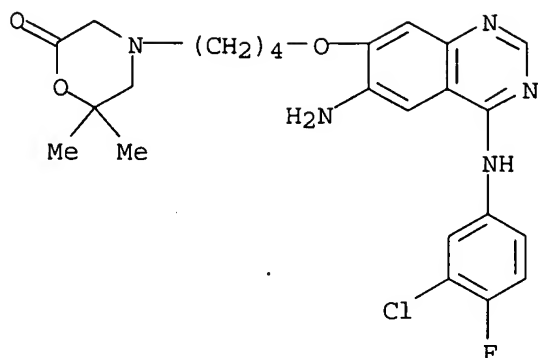
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



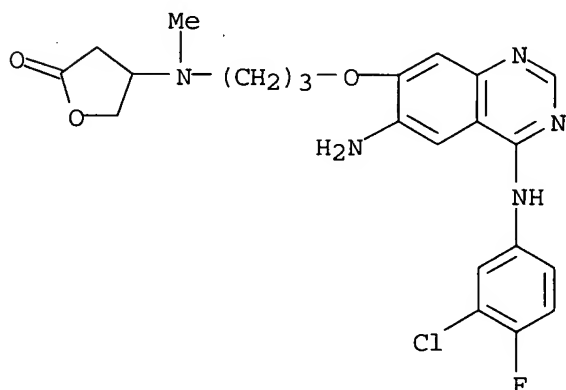
RN 402723-99-3 CAPLUS

CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)

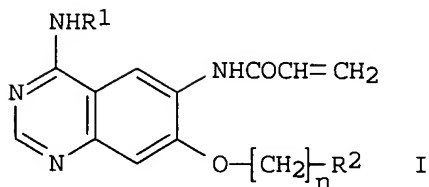


RN 402724-00-9 CAPLUS

CN 2(3H)-Furanone, 4-[[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]methylamino]dihydro- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = PhCH₂, 1-phenylethyl, (substituted) Ph; R2 = N-(2-oxotetrahydrofuran-4-yl)methylamino, N(CH₂CO₂R₃)₂, (substituted) R₄OCOCH₂NCH₂CH₂OH, 2-oxomorpholin-4-yl; R₃ = H, Me, Et; R₄ = H, alkyl; n = 2-4], were prep'd. Thus, a mixt. of CH₂:CHCO₂H and Et₃N was stirred for 1 h at -50.degree. with CH₂:CHCO₂Cl in THF followed by addn. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]quinazoline (prepn. given) in THF at -55.degree. and slowly heating up at 0.degree. up to completely conversion to give 60% 4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-

oxomorpholin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. One of the exemplified examples, 4-[(R)-(1-phenylethyl)amino]-7-[2-(2,2-dimethyl-6-oxomorpholin-4-yl)ethoxy]-6-[(vinylcarbonyl)amino]quinazoline, inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.4 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:171889 CAPLUS

DN 136:232315

TI Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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US 2002077330	A1	20020620	US 2001-929931	20010815
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			US 2000-230389PP	20000906
AU 2001084021	A5	20020313	AU 2001-84021	20010818
			DE 2000-10042060A	20000826
			WO 2001-EP9537 W	20010818
EP 1315717	A1	20030604	EP 2001-962953	20010818
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
			DE 2000-10042060A	20000826
			WO 2001-EP9537 W	20010818

OS MARPAT 136:232315

IT 290303-28-5P 290303-32-1P 290304-07-3P

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402855-01-0P 402855-03-2P 402855-04-3P

402855-05-4P

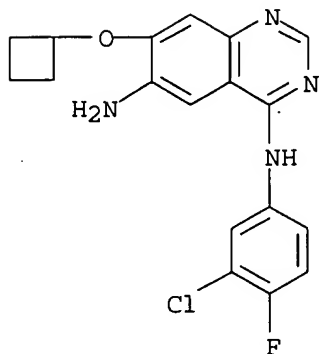
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (amino) (vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

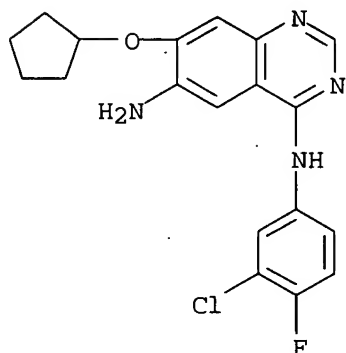
RN 290303-28-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutyloxy)-

(9CI) (CA INDEX NAME)

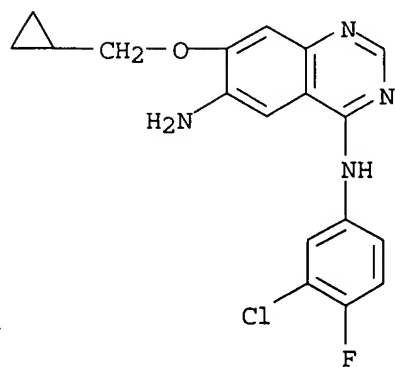


RN 290303-32-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopentyloxy)-
(9CI) (CA INDEX NAME)

RN 290304-07-3 CAPLUS

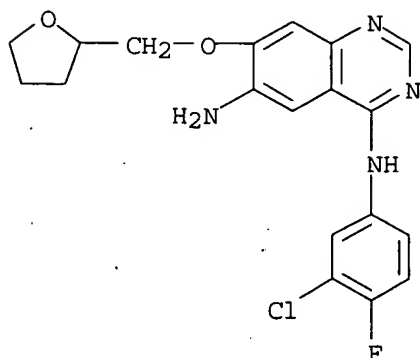
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



RN 314771-75-0 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2-

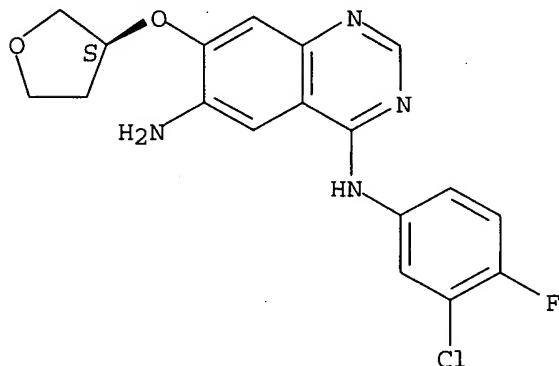
furanyl)methoxy] - (9CI) (CA INDEX NAME)



RN 314771-76-1 CAPLUS

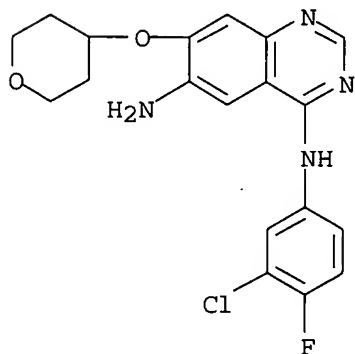
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[3-(3-furanyl)oxy] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



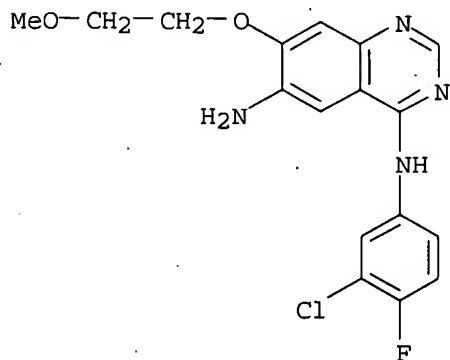
RN 314771-77-2 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)oxy] - (9CI) (CA INDEX NAME)



RN 402855-01-0 CAPLUS

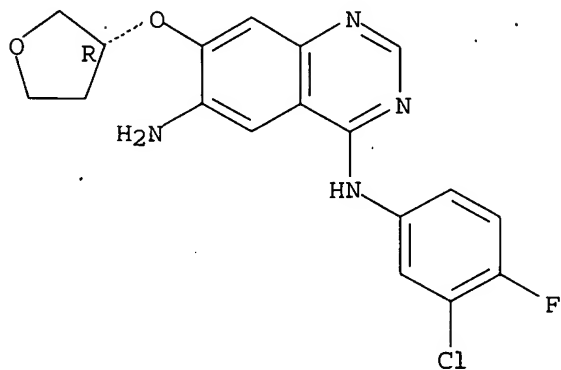
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(2-methoxyethoxy)-(9CI) (CA INDEX NAME)



RN 402855-03-2 CAPLUS

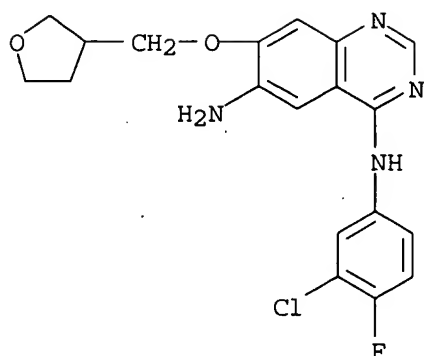
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3R)-tetrahydro-3-furanyl]oxy]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



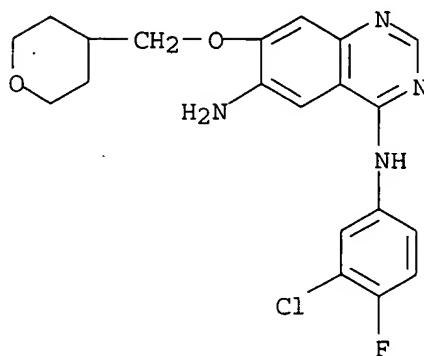
RN 402855-04-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-3-furanyl)methoxy]-(9CI) (CA INDEX NAME)

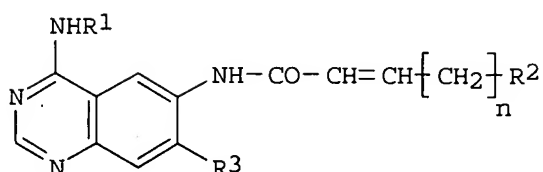


RN 402855-05-4 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)methoxy] - (9CI) (CA INDEX NAME)



GI



I

AB Title compds. [I; R1 = PhCH₂, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R₄OCOCH₂NCH₂CH₂OH, 2-oxomorpholin-4-yl; R₄ = H, alkyl; R₃ = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepd. Thus, a mixt. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and diisopropylethylamine in THF was dropwise treated under ice-cooling with BrCH₂CH:CHCO₂Cl (prepn. given) in CH₂Cl₂ followed by stirring for 1 h under ice-cooling and for 2 h at room temp. and addn. of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH₂Cl₂ to give after stirring over night at room temp. and stirring for 5 h at 60.degree.

64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2002:171886 CAPLUS

DN 136:216758

TI Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018370	A1	20020307	WO 2001-EP9535	20010818
	W:				
					AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
	RW:				GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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	DE 10042061	A1	20020307	DE 2000-10042061	20000826
	AU 2001089814	A5	20020313	AU 2001-89814	20010818
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				WO 2001-EP9535 W	20010818
	EP 1315716	A1	20030604	EP 2001-969610	20010818
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				WO 2001-EP9535 W	20010818
	US 2002082270	A1	20020627	US 2001-934753	20010822
				DE 2000-10042061A	20000826
				US 2000-230119PP	20000905

OS MARPAT 136:216758

IT 402496-48-4P 402496-50-8P 402496-52-0P

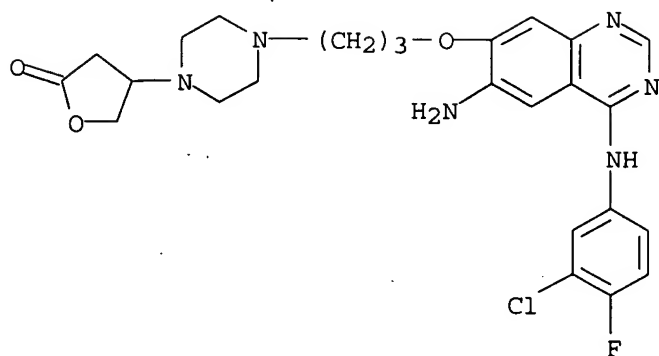
402496-81-5P 402496-83-7P 402497-08-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (amino) (heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402496-48-4 CAPLUS

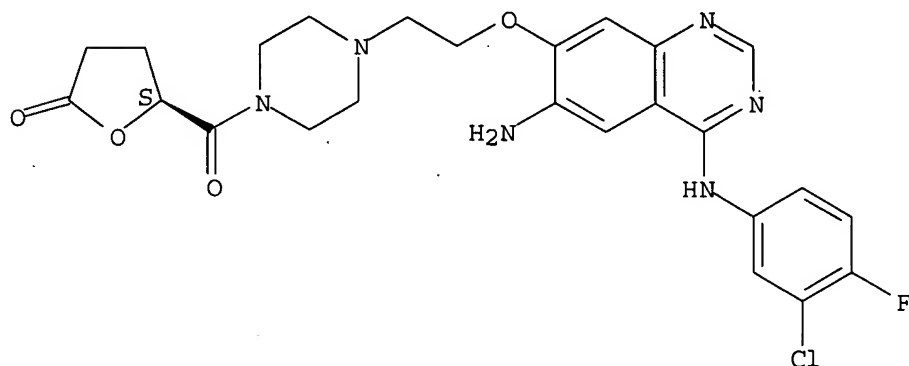
CN 2(3H)-Furanone, 4-[4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)



RN 402496-50-8 CAPLUS

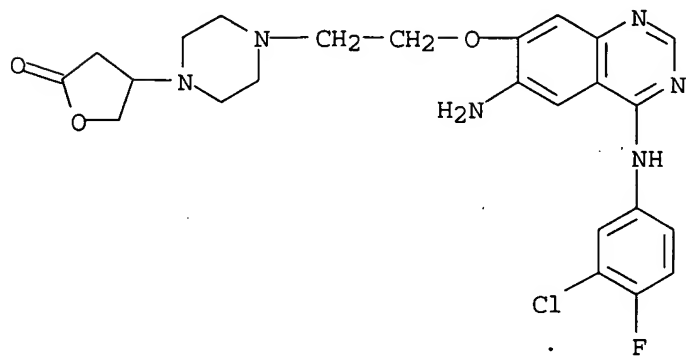
CN Piperazine, 1-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-4-[[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402496-52-0 CAPLUS

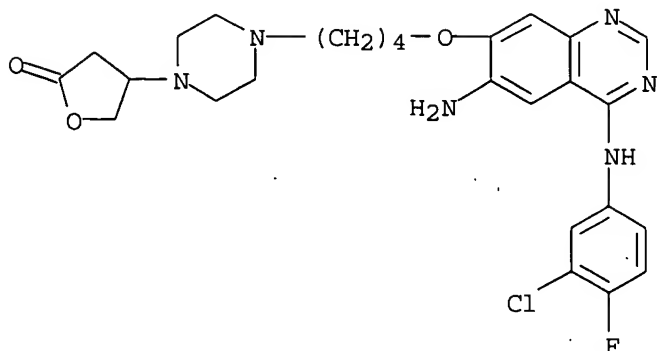
CN 2(3H)-Furanone, 4-[4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)



RN 402496-81-5 CAPLUS

CN 2(3H)-Furanone, 4-[4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-

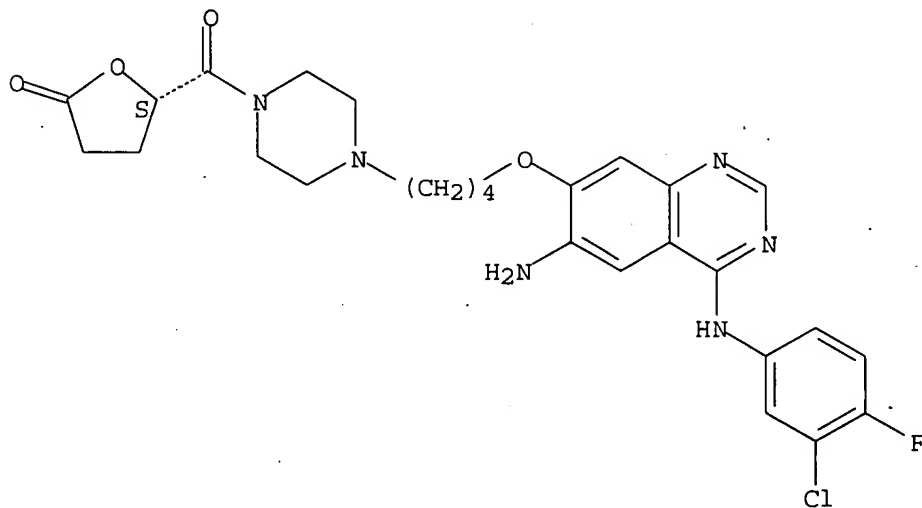
quinazolinyl]oxy]butyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)



RN 402496-83-7 CAPLUS

CN Piperazine, 1-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-4-[[2S]-tetrahydro-5-oxo-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)

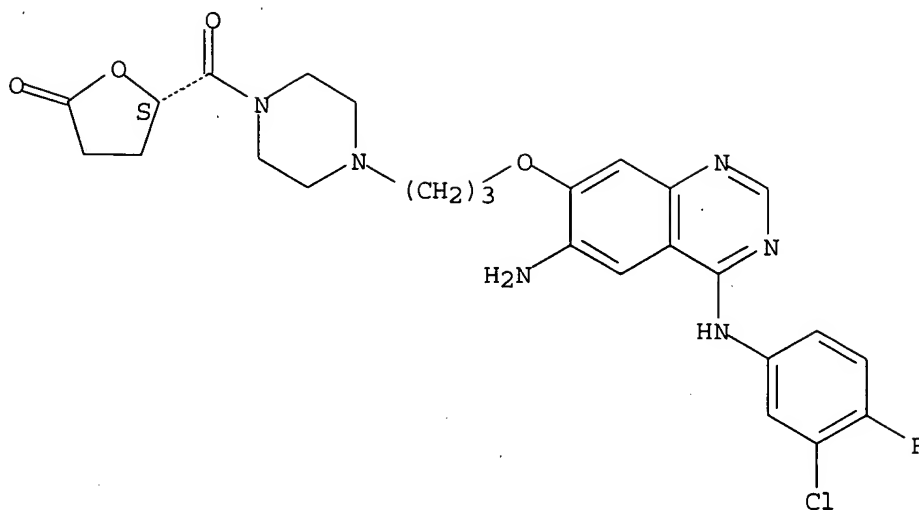
Absolute stereochemistry.



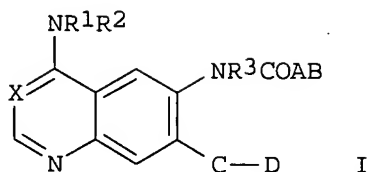
RN 402497-08-9 CAPLUS

CN Piperazine, 1-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-4-[[2S]-tetrahydro-5-oxo-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH₂, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = H, (substituted) alkyl, alkylcarbonyl, CO₂H, alkoxycarbonyl, aminocarbonyl, (di)alkylaminocarbonyl, pyrrolidinylcarbonyl, piperidinylcarbonyl, morpholinocarbonyl, alkylpiperazinylcarbonyl; C = (oxy)alkenyl, O; D = (substituted) pyrrolidinyl, piperidinyl, hexahydroazepinyl, piperazinyl, etc.], were prepd. Thus, a mixt. of CH₂:CHCO₂H and Et₃N was stirred for 45 min at -50.degree. with CH₂:CHCO₂Cl in THF followed by dropwise addn. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)quinazoline (prepn. given) in THF for 20 min and stirring at 0.degree. up to completely conversion to give 31% 4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 12 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4. ANSWER 7 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2001:762992 CAPLUS
DN 135:303907

Patel

<7/1/2003>

TI Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.
 IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
 PA Boehringer Ingelheim Pharma K.-G., Germany
 SO PCT Int. Appl., 95 pp.
 CODEN: PIXXD2
 DT Patent
 LA German
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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	DE 10040525	A1	20020228	DE 2000-10040525A	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
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				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

PATENT FAMILY INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FAN	2001:747043				
PI	DE 10017539	A1	20011011	DE 2000-10017539	20000408
	US 2001044435	A1	20011122	US 2001-816003	20010323
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	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
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				DE 2000-10040525A	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
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				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

OS MARPAT 135:303907

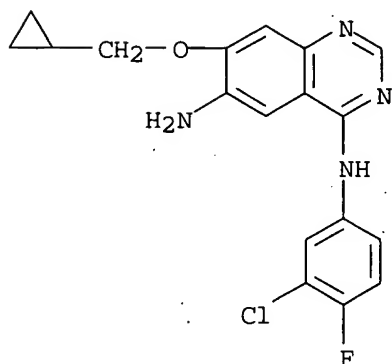
IT 290304-07-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

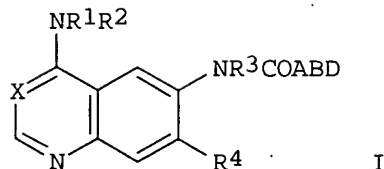
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 290304-07-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy) - (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (prepn. given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temp. to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.05 nM.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2001:747043 CAPLUS

DN 135:303901

TI Bicyclic heterocycles as inhibitors of epidermal growth factor receptor

mediated signal transduction

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10017539	A1	20011011	DE 2000-10017539	20000408
US 2001044435	A1	20011122	US 2001-816003	20010323
			DE 2000-10017539A	20000408
			DE 2000-10040525A	20000818
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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EP 1280798	A1	20030205	EP 2001-938076	20010331
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PATENT FAMILY INFORMATION:

FAN 2001:762992

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DE 10017539	A1	20011011	DE 2000-10017539	20000408
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OS MARPAT 135:303901

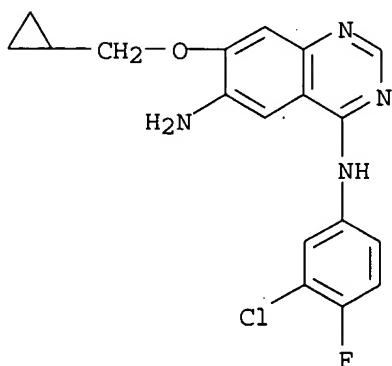
IT 290304-07-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

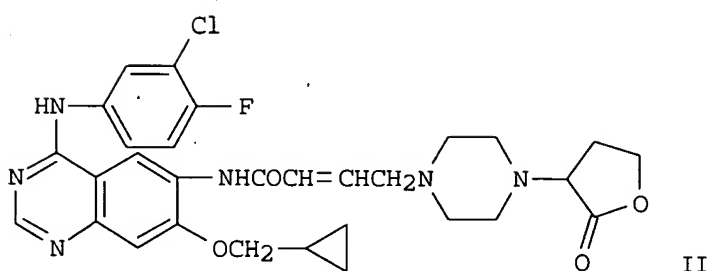
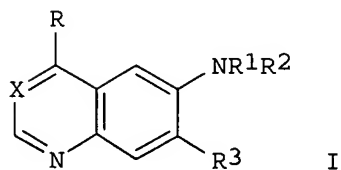
(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 290304-07-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



GI



AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH₂; R₁ = H, alkyl; R₂ = acyl; R₃ = H, (un)substituted alkoxy, cycloalkoxy, tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepd. for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by redn. to the amine, reaction with 4-bromocrotonic acid and N-tert.-

butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2001:636060 CAPLUS

DN 135:211054

TI Method for the simplified production of N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]-amine

IN Barth, Hubert; Steiner, Klaus; Schneider, Simon

PA Goedecke G.m.b.H., Germany

SO PCT Int. Appl., 13 pp.

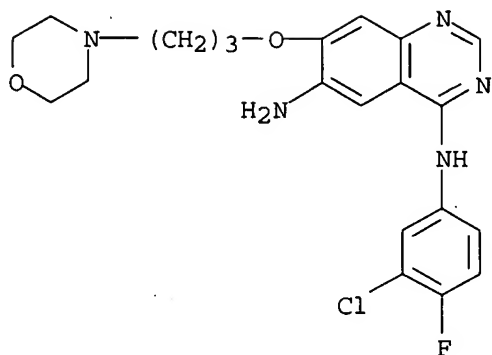
CODEN: PIXXD2

DT Patent

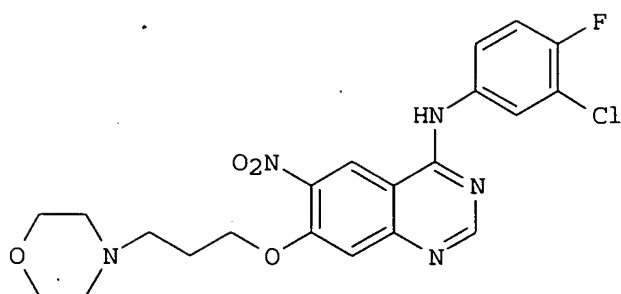
LA German

FAN. CNT 1

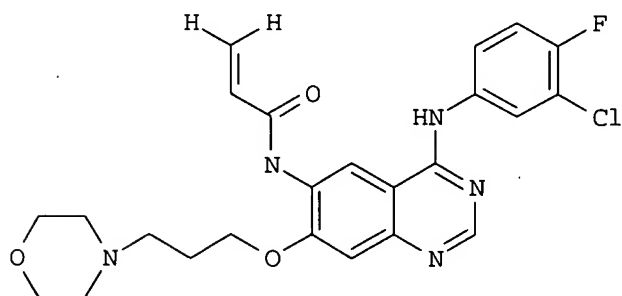
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PI	WO 2001062743	A2	20010830	WO 2001-EP695	20010123
	WO 2001062743	A3	20020314		
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	AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
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	DE 10009267	A1	20010830	DE 2000-10009267A	20000226
	BR 2001008695	A	20021210	DE 2000-10009267	20000226
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				DE 2000-10009267A	20000226
				WO 2001-EP695 W	20010123
	EP 1265874	A2	20021218	EP 2001-953631	20010123
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				DE 2000-10009267A	20000226
				WO 2001-EP695 W	20010123
	US 2003050313	A1	20030313	US 2002-204911	20020826
				DE 2000-10009267A	20000226
				WO 2001-EP695 W	20010123
OS	CASREACT 135:211054				
IT	267243-68-5P				
	RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)				
	(method for the simplified prodn. of N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]-amine)				
RN	267243-68-5 CAPLUS				
CN	4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)				



GI



I



II

AB N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine (I) or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]amine (II) are prepd. in high yield and selectivity by the chlorination of 7-fluoro-6-nitroquinazolin-4(3H)-one with thionyl chloride to give 4-chloro-7-fluoro-6-nitroquinazoline which is condensed with 3-(4-morpholinyl)-1-propanol to give I which is then hydrogenated (e.g., using Raney nickel) into II.

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2001:380438 CAPLUS

DN 135:24657

TI Selective cellular targeting: multifunctional delivery vehicles

IN Glazier, Arnold

PA Drug Innovation + Design, Inc., USA

SO PCT Int. Appl., 981 pp.

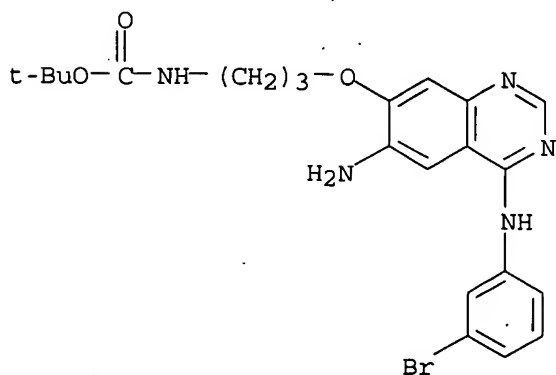
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001036003	A2	20010525	WO 2000-US31262	20001114
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
AU 2001016075	A5	20010530	AU 2001-16075	20001114
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
			WO 2000-US31262W	20001114
EP 1255567	A1	20021113	EP 2000-978631	20001114
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
			WO 2000-US31262W	20001114
IT 341551-80-2P				
RL:	PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)			
	(multifunctional delivery vehicles for selective cellular targeting of drugs)			
RN 341551-80-2	CAPLUS			
CN	Carbamic acid, [3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)			



AB The present invention relates to the compns., methods, and applications of a novel approach to selective cellular targeting. The purpose of this invention is to enable the selective delivery and/or selective activation of effector mols. to target cells for diagnostic or therapeutic purposes. The present invention relates to multi-functional prodrugs or targeting vehicles wherein each functionality is capable of enhancing targeting selectivity, affinity, intracellular transport, activation or detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for cancer treatment.

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:911231 CAPLUS

DN 134:71599

TI Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.

IN Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 104 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000078735	A1	20001228	WO 2000-EP5547	20000616
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
			DE 1999-19928281A	19990621
			US 1999-146644PP	19990730
			DE 2000-10023085A	20000511
DE 19928281	A1	20001228	DE 1999-19928281	19990621
DE 10023085	A1	20011115	DE 2000-10023085	20000511
BR 2000011834	A	20020312	BR 2000-11834	20000616
			DE 1999-19928281A	19990621
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			WO 2000-EP5547 W	20000616
EP 1194418	A1	20020410	EP 2000-936888	20000616
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
			DE 1999-19928281A	19990621
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			WO 2000-EP5547 W	20000616
JP 2003502410	T2	20030121	JP 2001-504901	20000616
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			US 1999-146644PP	19990730
			DE 2000-10023085A	20000511
			WO 2000-EP5547 W	20000616
EE 200100695	A	20030217	EE 2001-695	20000616

			DE 1999-19928281A 19990621
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
BG 106189	A	20020830	WO 2000-EP5547 W 20000616
			BG 2001-106189 20011207
			DE 1999-19928281A 19990621
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
			WO 2000-EP5547 W 20000616
US 2002169180	A1	20021114	US 2001-16280 20011210
			DE 1999-19928281A 19990621
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			DE 2000-10023085A 20000511
NO 2001006185	A	20011218	NO 2001-6185 20011218
			DE 1999-19928281A 19990621
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
			WO 2000-EP5547 W 20000616

OS MARPAT 134:71599

IT 290303-28-5P 290303-32-1P 290304-07-3P

314771-70-5P 314771-71-6P 314771-72-7P

314771-73-8P 314771-74-9P 314771-75-0P

314771-76-1P 314771-77-2P 314771-80-7P

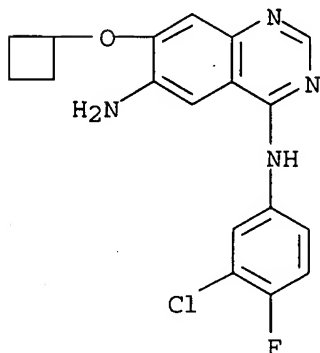
314771-81-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors)

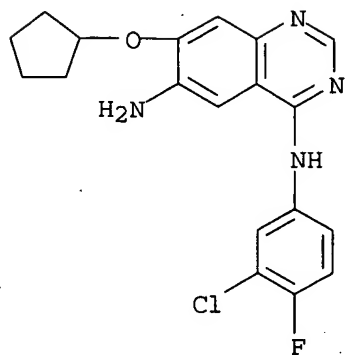
RN 290303-28-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutyloxy) - (9CI) (CA INDEX NAME)



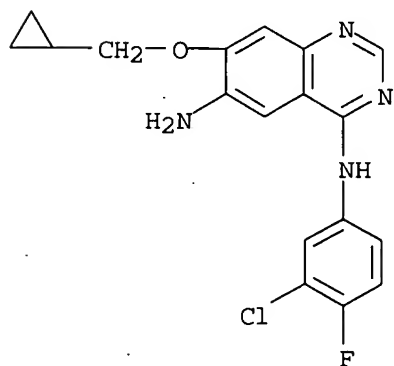
RN 290303-32-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopentyloxy) - (9CI) (CA INDEX NAME)



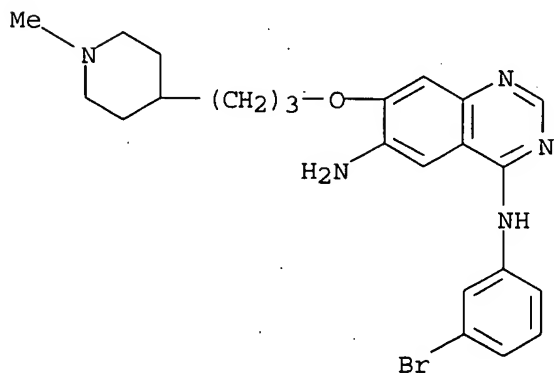
RN 290304-07-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



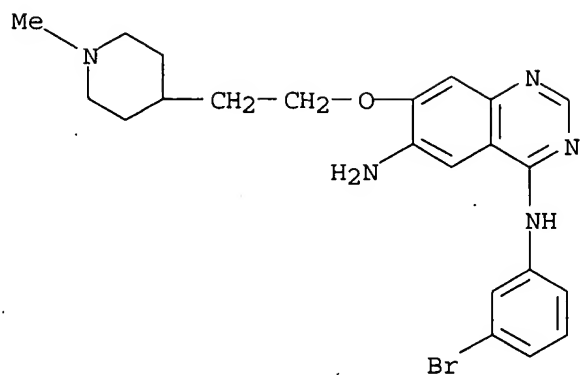
RN 314771-70-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1-methyl-4-piperidinyl)propoxy]- (9CI) (CA INDEX NAME)



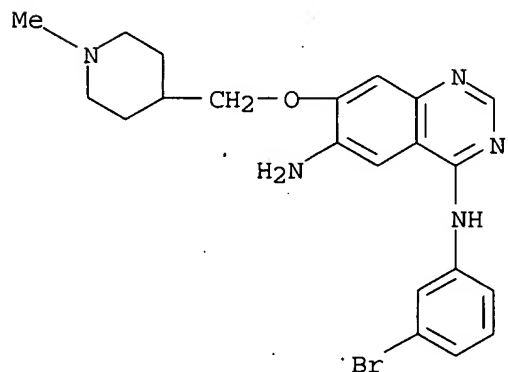
RN 314771-71-6 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[2-(1-methyl-4-piperidinyl)ethoxy]- (9CI) (CA INDEX NAME)



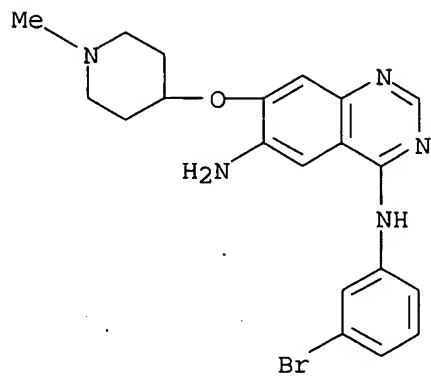
RN 314771-72-7 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[(1-methyl-4-piperidiny)methoxy] - (9CI) (CA INDEX NAME)



RN 314771-73-8 CAPLUS

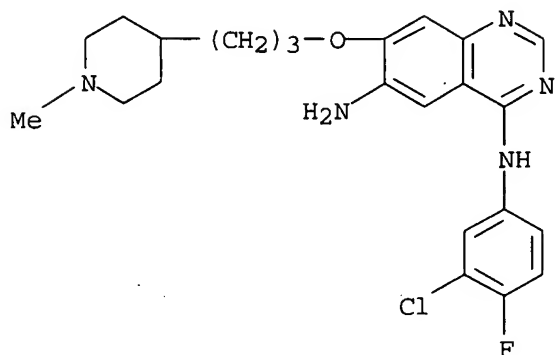
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[(1-methyl-4-piperidiny)oxy] - (9CI) (CA INDEX NAME)



RN 314771-74-9 CAPLUS

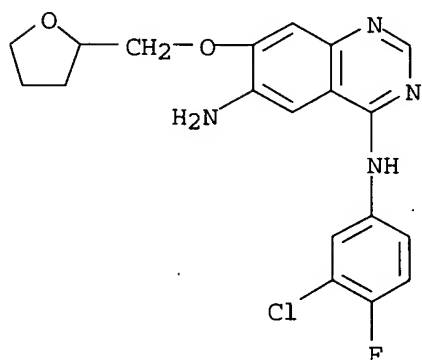
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(1-methyl-4-piperidiny)oxy] - (9CI) (CA INDEX NAME)

piperidinyl)propoxy] - (9CI) (CA INDEX NAME)



RN 314771-75-0 CAPLUS

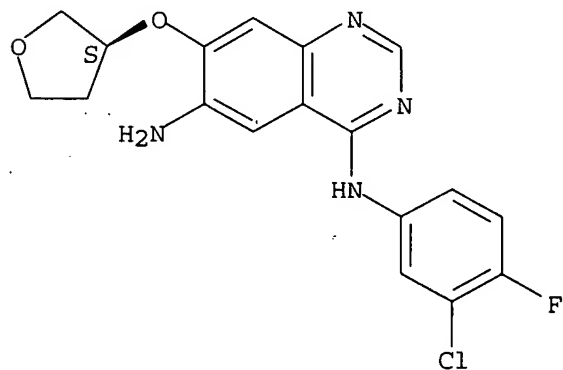
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2-furanyl)methoxy] - (9CI) (CA INDEX NAME)



RN 314771-76-1 CAPLUS

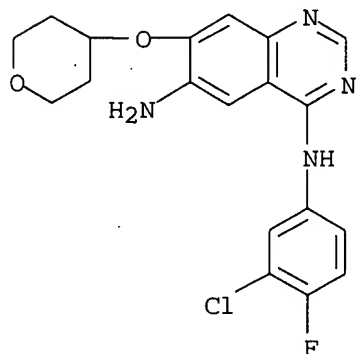
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-furanyl]oxy] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



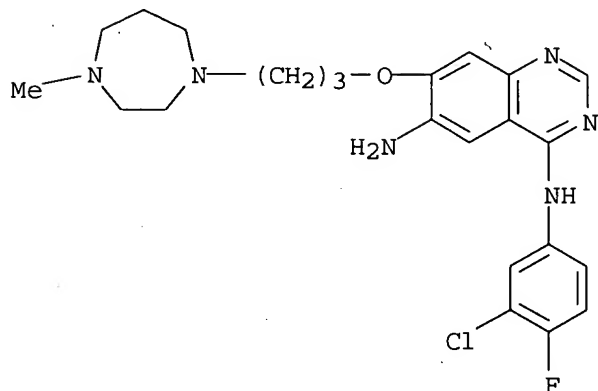
RN 314771-77-2 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)oxy] - (9CI) (CA INDEX NAME)



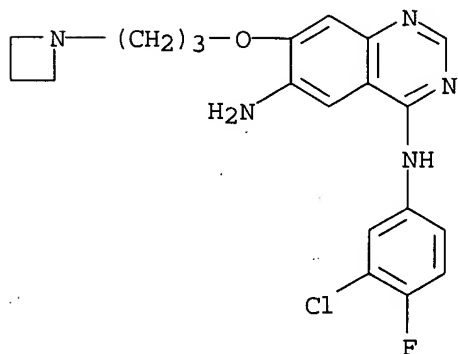
RN 314771-80-7 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)propoxy] - (9CI) (CA INDEX NAME)

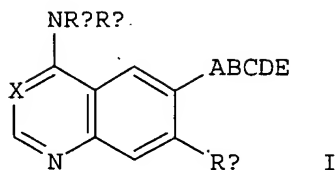


RN 314771-81-8 CAPLUS

CN 4,6-Quinazolinediamine, 7-[3-(1-azetidiny)propoxy]-N4-(3-chloro-4-fluorophenyl) - (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH₂, PhCH₂CH₂; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO₂; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxy]quinazoline (prepn. given) in CH₂Cl₂ contg. Et₃N at -10.degree. was treated with acryloyl chloride in THF to give 35% 4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with IC₅₀ = <0.35 nM.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:628125 CAPLUS

DN 133:207919

TI Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 232 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224
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			US 1999-149329PP	19990817
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DE 19908567	A1	20000831	DE 1999-19908567	19990227
DE 19911366	A1	20000921	DE 1999-19911366	19990315
DE 19928306	A1	20001228	DE 1999-19928306	19990621
DE 19954816	A1	20010517	DE 1999-19954816	19991113
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EP 1157011	A1	20011128	EP 2000-910695	20000224
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			WO 2000-EP1496 W	20000224
BR 2000008524	A	20011218	BR 2000-8524	20000224
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			DE 1999-19928306A	19990621
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			WO 2000-EP1496 W	20000224
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EE 200100449	A	20021216	EE 2001-449	20000224
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			DE 1999-19911366A	19990315
			DE 1999-19928306A	19990621
			US 1999-149329PP	19990817
			DE 1999-19954816A	19991113
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BG 105765	A	20020329	BG 2001-105765	20010801
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NO 2001004114	A	20011015	NO 2001-4114	20010824
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			DE 1999-19911366A	19990315

DE 1999-19928306A 19990621
 US 1999-149329PP 19990817
 DE 1999-19954816A 19991113
 WO 2000-EP1496 W 20000224

PATENT FAMILY INFORMATION:

FAN 2000:607393

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908567	A1	20000831	DE 1999-19908567	19990227
CA 2361174	AA	20000908	CA 2000-2361174	20000224
			DE 1999-19908567A	19990227
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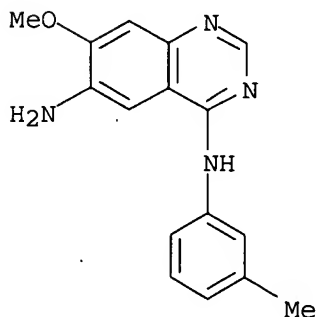
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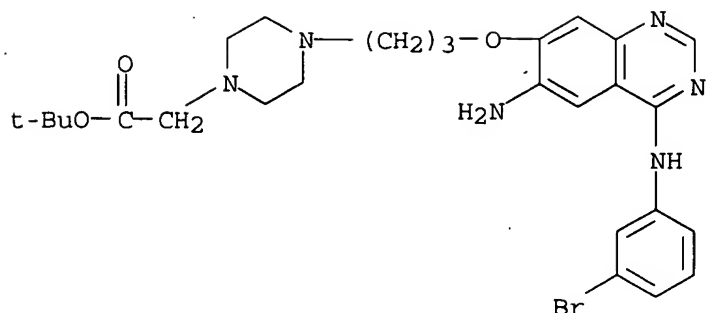
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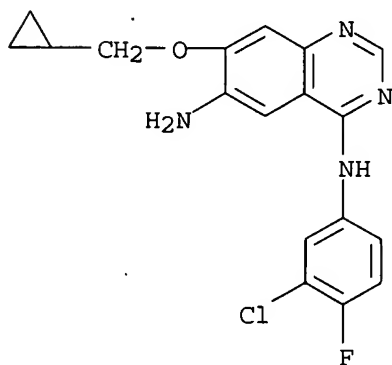
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CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 290304-07-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)-(9CI) (CA INDEX NAME)



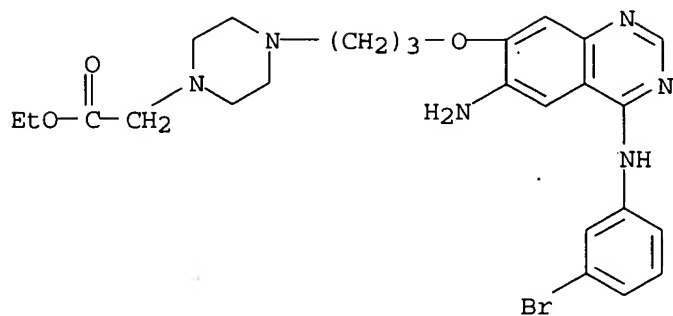
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

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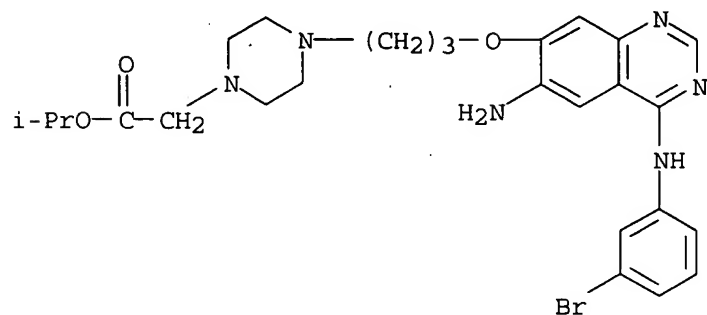
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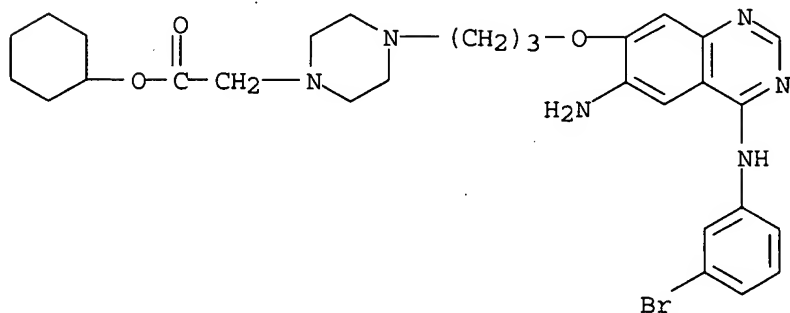
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CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



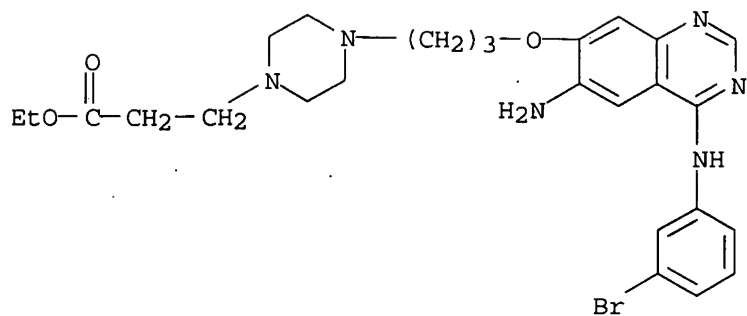
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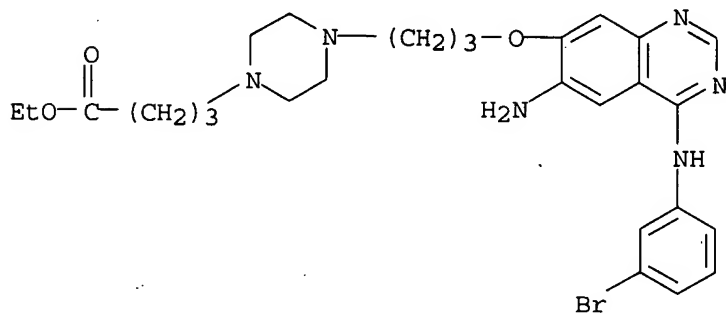
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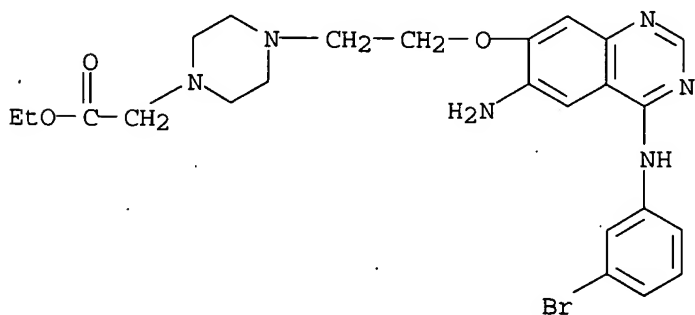
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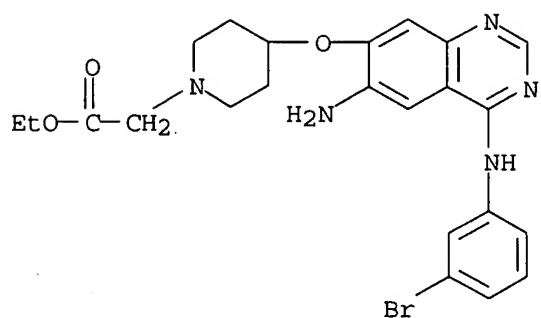
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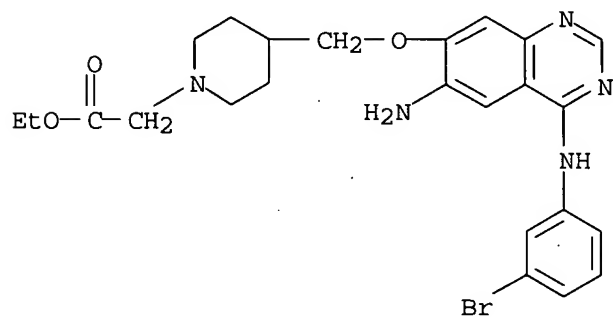
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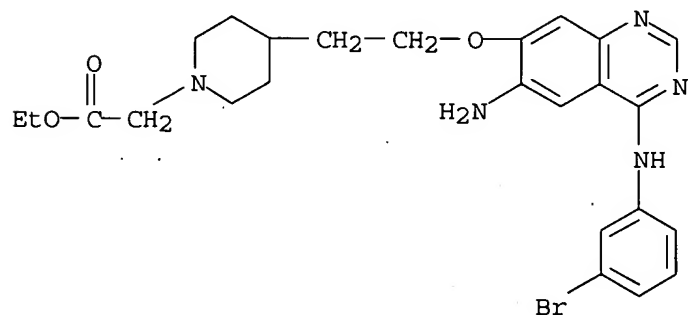
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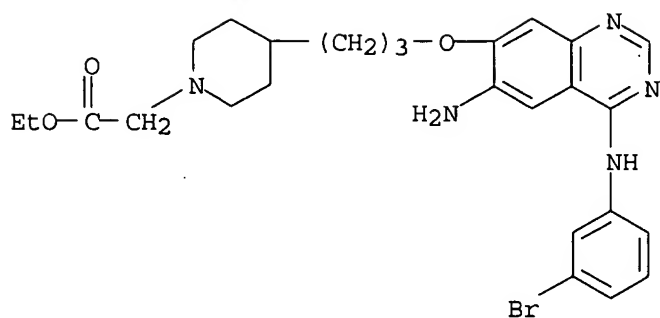
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CN 1-Piperidineacetic acid, 4-[2-[[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



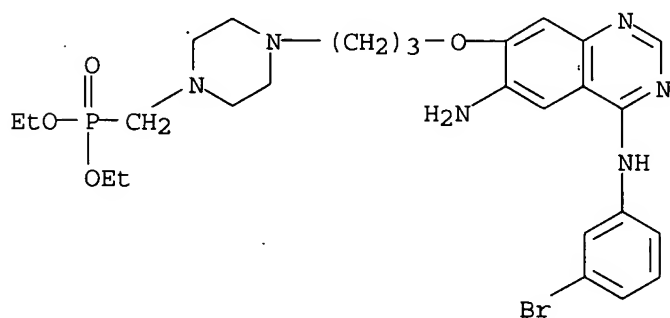
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CN 1-Piperidineacetic acid, 4-[3-[[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



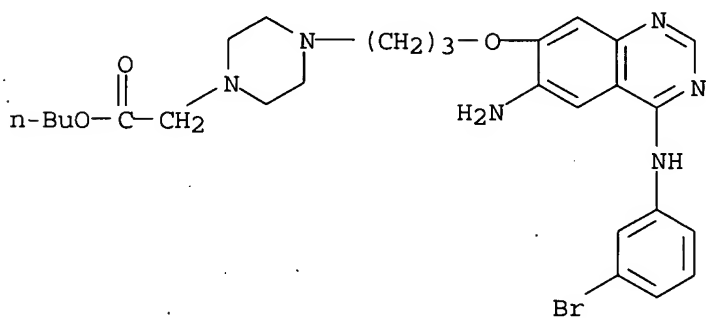
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CN Phosphonic acid, [[4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-1-piperazinyl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



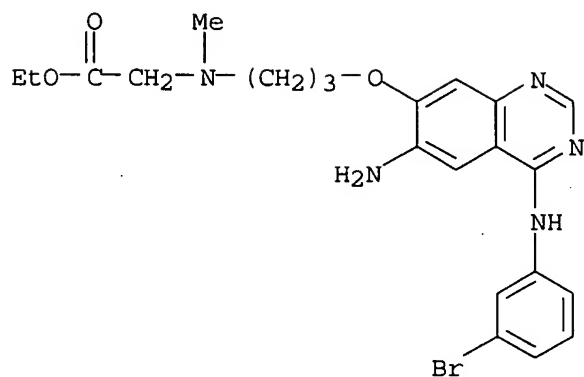
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CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, butyl ester (9CI) (CA INDEX NAME)



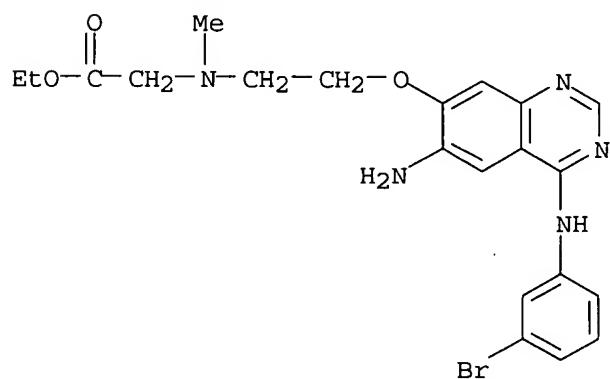
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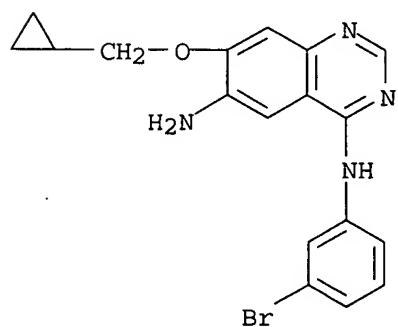
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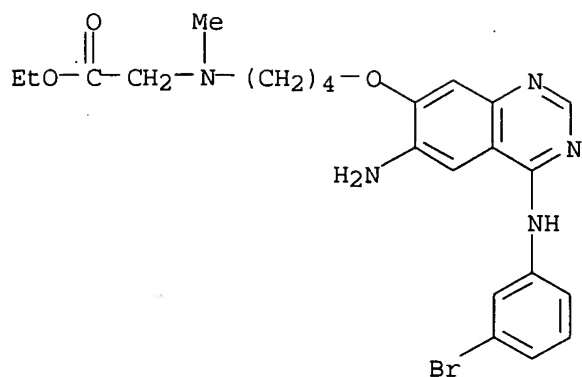
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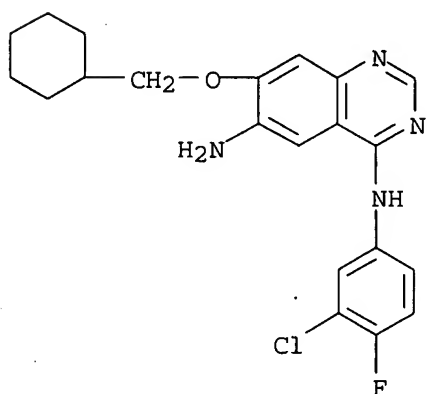


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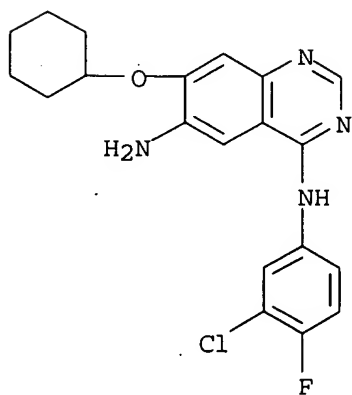
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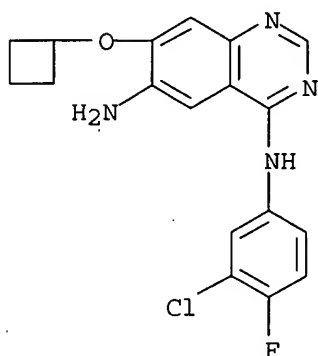
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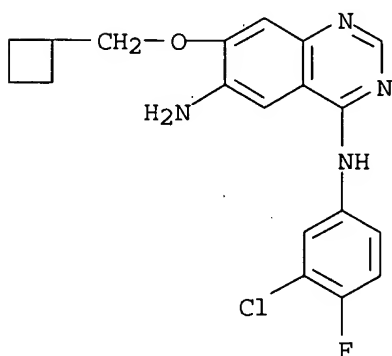
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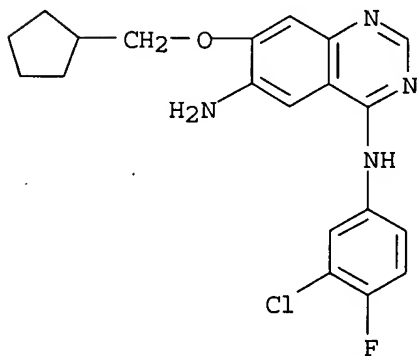
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RN 290303-30-9 CAPLUS

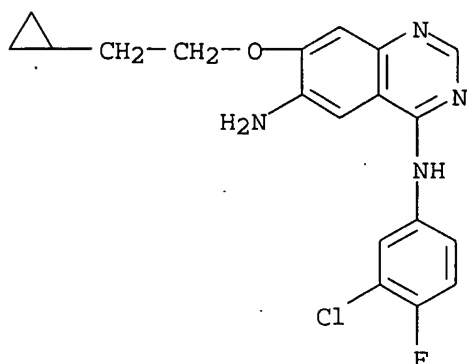
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RN 290303-31-0 CAPLUS

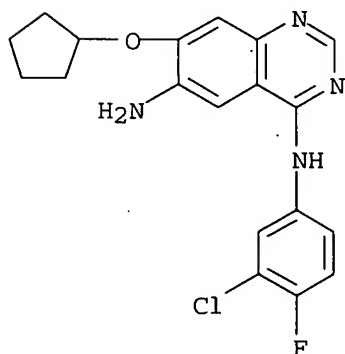
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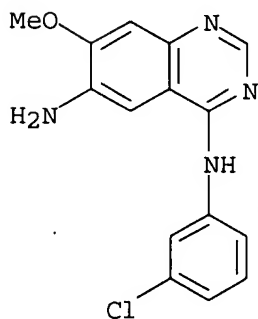
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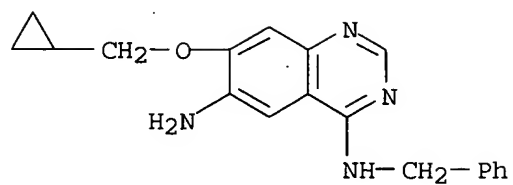
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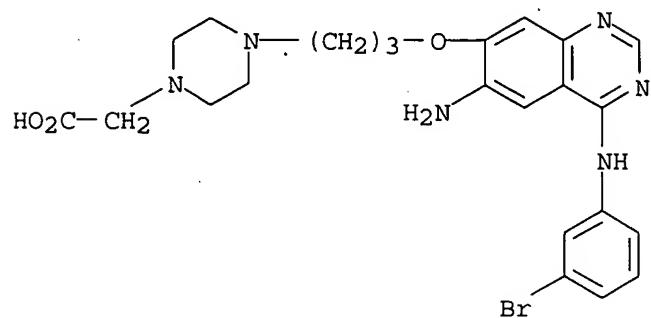
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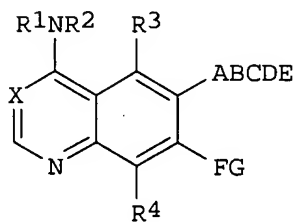


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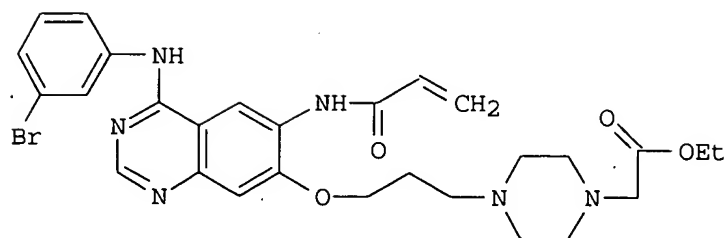
CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]- (9CI) (CA INDEX NAME)



GI



I



II

AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D = alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepd. and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compd. II was prepd. and tested by Cell Titer 96TM Aq. Nonradioactive Cell Proliferation Assay.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:607393 CAPLUS

DN 133:207916

TI Preparation of aminoquinazolines as epidermal growth factor receptor inhibitors.

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas

PA Boehringer Ingelheim Pharma K-G, Germany

SO Ger. Offen., 26 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 2

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BR 2000008524 A 20011218

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PATENT FAMILY INFORMATION:

FAN 2000:628125

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 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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 DE 1999-19911366A 19990315
 DE 1999-19928306A 19990621
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 IE, SI, LT, LV, FI, RO
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HR 20010617 A1 20021031

NO 2001004114 A 20011015

US 1999-149329PP 19990817
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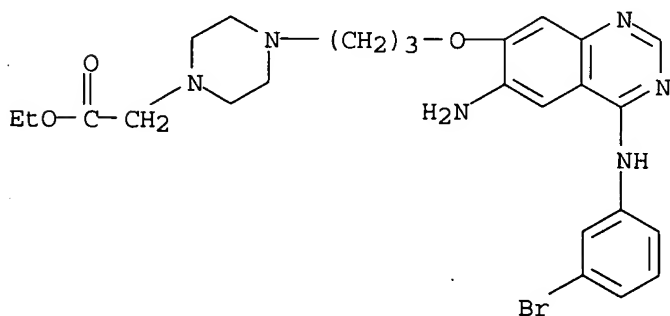
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IT 289700-72-7P 289700-73-8P 289700-74-9P
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 289700-81-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (prepn. of aminoquinazolines as epidermal growth factor receptor
 inhibitors)

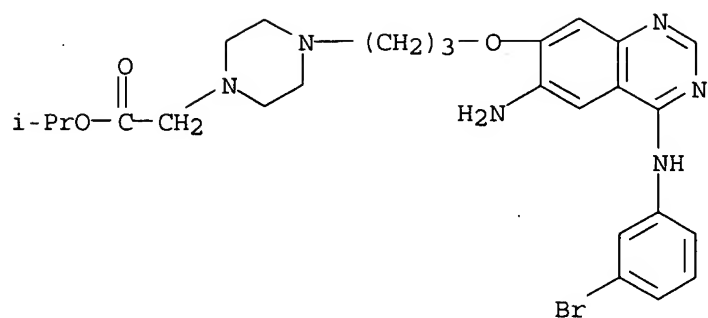
RN 289700-72-7 CAPLUS

CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-
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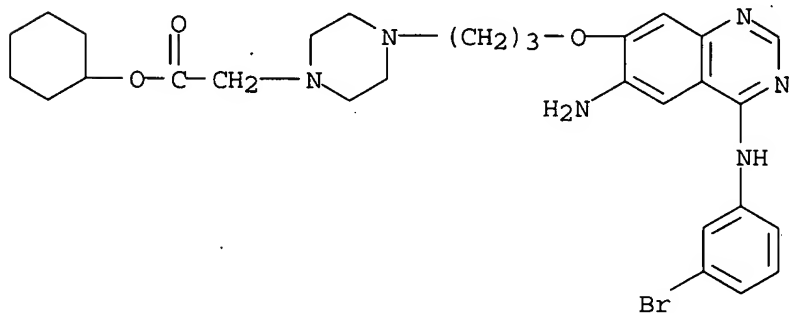
RN 289700-73-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-
 quinazolinyl]oxy]propyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



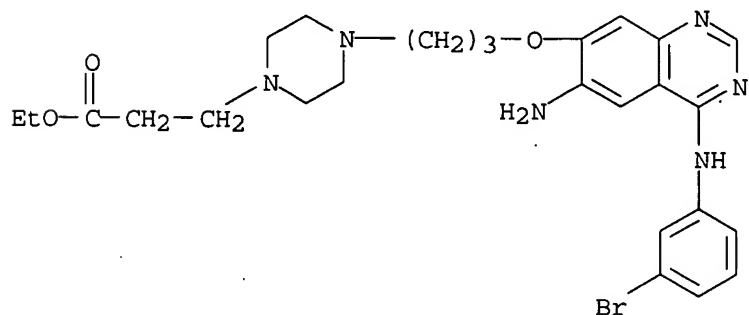
RN 289700-74-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, cyclohexyl ester (9CI) (CA INDEX NAME)



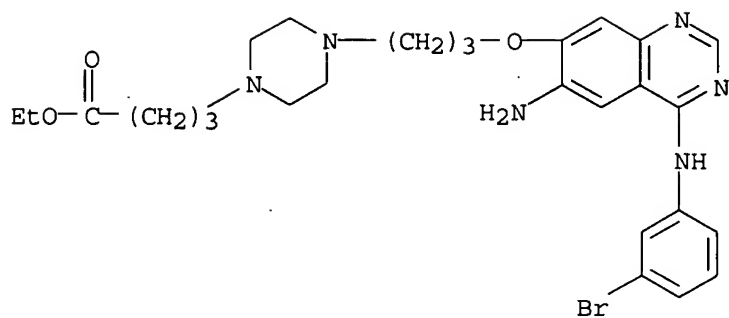
RN 289700-75-0 CAPLUS

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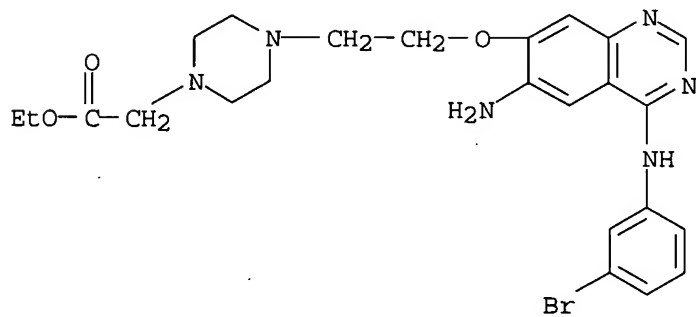
RN 289700-76-1 CAPLUS

CN 1-Piperazinebutanoic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



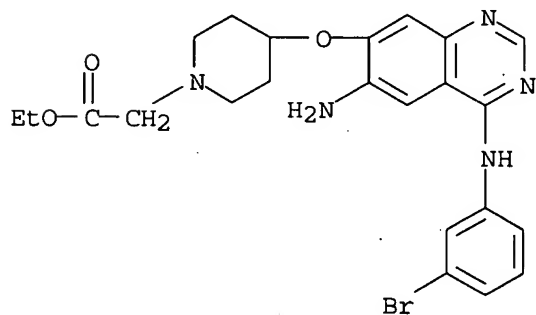
RN 289700-77-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[2-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



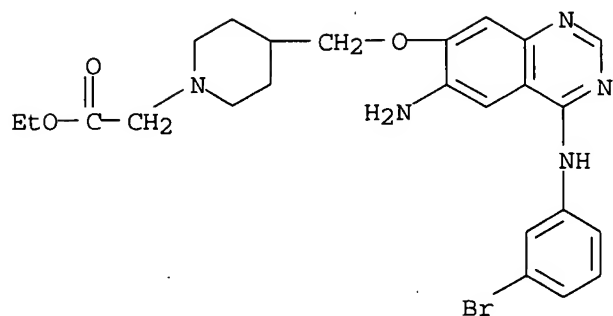
RN 289700-78-3 CAPLUS

CN 1-Piperidineacetic acid, 4-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



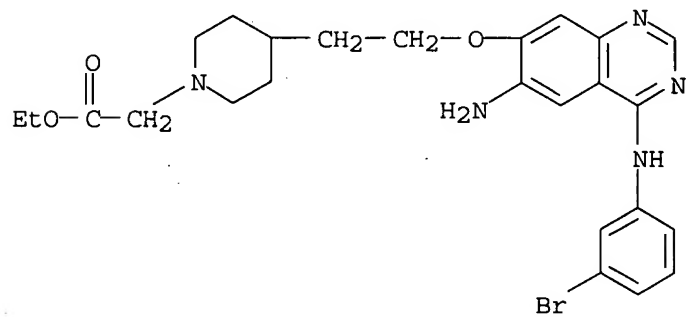
RN 289700-79-4 CAPLUS

CN 1-Piperidineacetic acid, 4-[[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



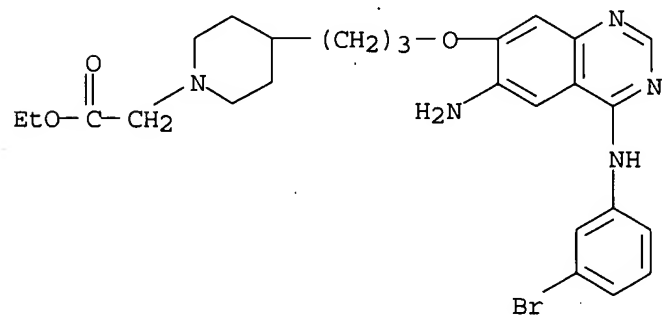
RN 289700-80-7 CAPLUS

CN 1-Piperidineacetic acid, 4-[2-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

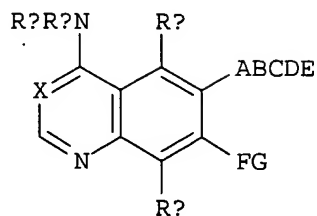


RN 289700-81-8 CAPLUS

CN 1-Piperidineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH₂, 1-phenylethyl; Rc, Rm = H, F, Cl, MeO, (methoxy-, dimethylamino-, diethylamino-, pyrrolidino-, piperidino-, morpholino- substituted) Me; X = N, NCC; A = O, alkylimino; B = CO, SO₂; C = (Me- or F₃C-substituted) allenylene, vinylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, etc.; E, G = (substituted) R₆O₂CYNR₅, etc.; R₅ = H, (substituted) alkyl; R₆ = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, etc.; F = alkylene, oxyalkylene, O; FG = H, F, Cl, alkoxy, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-[4-(ethoxycarbonyl)methylpiperazin-1-yl]propoxy]quinazoline (prepn. given) in CH₂Cl₂ contg. Et₃N was treated with acryloyl chloride in CH₂Cl₂ at -10.degree. to give 62% 4-[(3-bromophenyl)amino]-7-[3-[4-[(ethoxycarbonyl)methyl]piperazin-1-yl]propoxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation with IC₅₀ = 2.6 nM.

L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:481416 CAPLUS

DN 134:216784

TI Tyrosine kinase inhibitors. 17. Irreversible inhibitors of the epidermal growth factor receptor: 4-(phenylamino)quinazoline- and 4-(phenylamino)pyrido[3,2-d]pyrimidine-6-acrylamides bearing additional solubilizing functions. [Erratum to document cited in CA132:317628]

AU Smaill, Jeff B.; Rewcastle, Gordon W.; Bridges, Alexander J.; Zhou, Hairong; Showalter, H. D. Hollis; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Elliott, William L.; Vincent, Patrick W.; DeJohn, Dana E.; Loo, Joseph A.; Greis, Kenneth D.; Chan, O. Helen; Reyner, Eric L.; Lipka, Elke; Denny, William A.

CS Auckland Cancer Society Research Centre, Faculty Medical and Health Sciences, The Univ. Auckland, Auckland, N. Z.

SO Journal of Medicinal Chemistry (2000), 43(16), 3199
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT 198961-78-3P 198961-84-1P 198961-86-3P

198961-87-4P 267243-67-4P 267243-68-5P

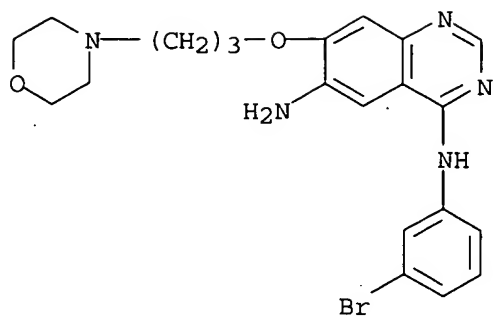
267243-69-6P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(antitumor and EGFR enzyme-inhibiting SAR of quinazolines (Erratum))

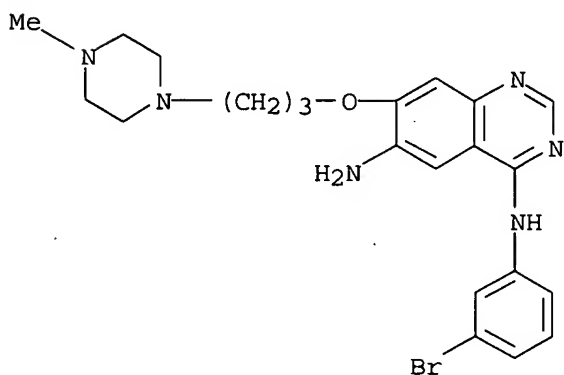
RN 198961-78-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-
(9CI) (CA INDEX NAME)



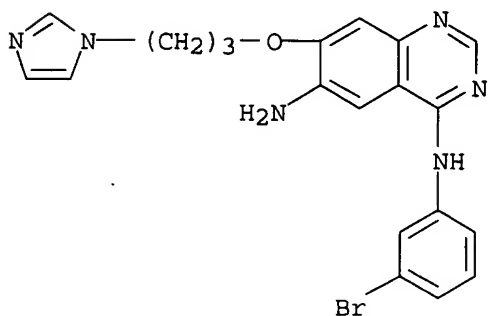
RN 198961-84-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy] - (9CI) (CA INDEX NAME)



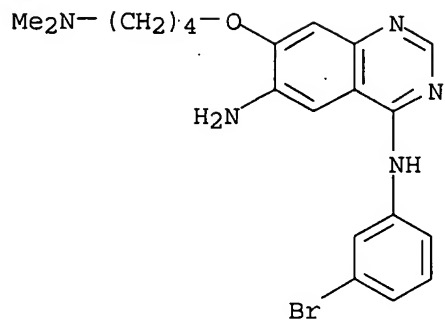
RN 198961-86-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy] - (9CI) (CA INDEX NAME)



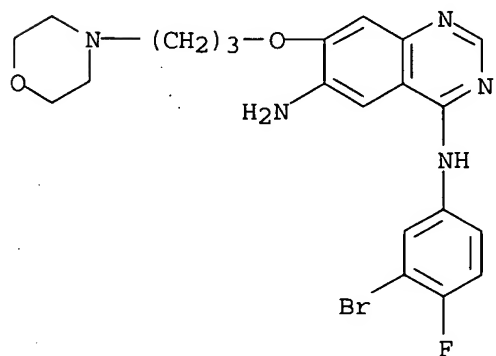
RN 198961-87-4 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy] - (9CI) (CA INDEX NAME)



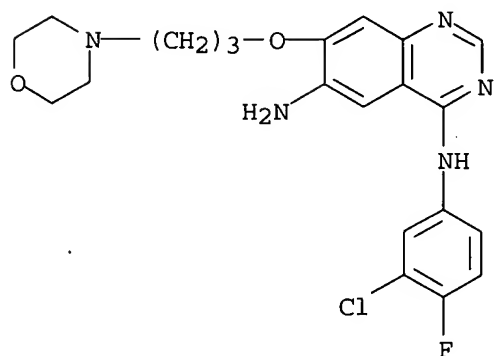
RN 267243-67-4 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromo-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy] - (9CI) (CA INDEX NAME)



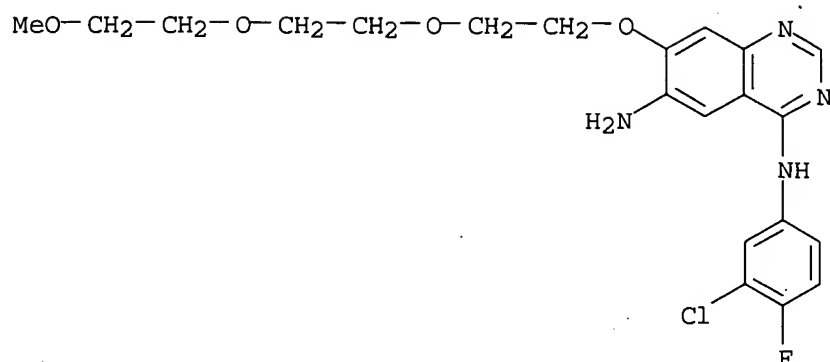
RN 267243-68-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy] - (9CI) (CA INDEX NAME)



RN 267243-69-6 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy] - (9CI) (CA INDEX NAME)

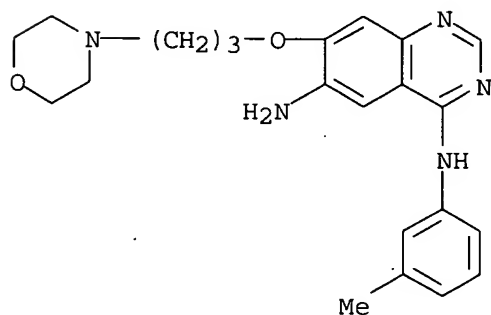


IT 198961-80-7P 198961-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines (Erratum))

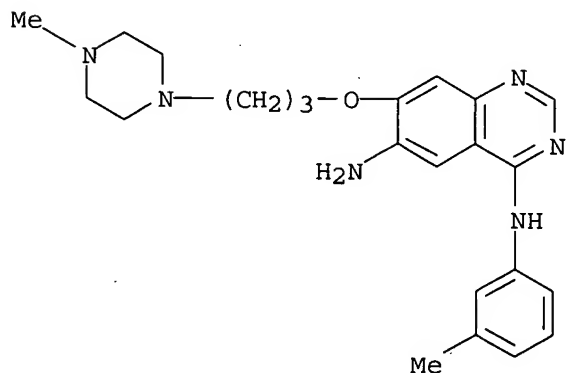
RN 198961-80-7 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 198961-82-9 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



AB Six author names were inadvertently omitted from the author contribution

Patel

<7/1/2003>

line. The complete author list is as follows: Jeff B. Smaill, Gordon W. Rewcastle, Alexander J. Bridges, Hairong Zhou, H. D. Hollis Showalter, David W. Fry, James M. Nelson, Veronika Sherwood, William L. Elliott, Patrick W. Vincent, Dana E. DeJohn, Joseph A. Loo, Kenneth D. Greis, O. Helen Chan, Eric L. Reyner, Elke Lipka, and William A. Denny.

L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:368316 CAPLUS

DN 133:4672

TI Preparation of N-{4-(3-chloro-4-fluorophenylamino)-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl}acrylamide as an irreversible inhibitor of tyrosine kinases

IN Bridges, Alexander James; Driscoll, Denise; Klohs, Wayne Daniel

PA Warner-Lambert Co., USA

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031048	A1	20000602	WO 1999-US22116	19990923
W:	AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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AT 229008	E	20021215	WO 1999-US22116W	19990923
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			US 1998-109065PP	19981119
US 6344455	B1	20020205	WO 1999-US22116W	19990923
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WO 1999-US22116W 19990923

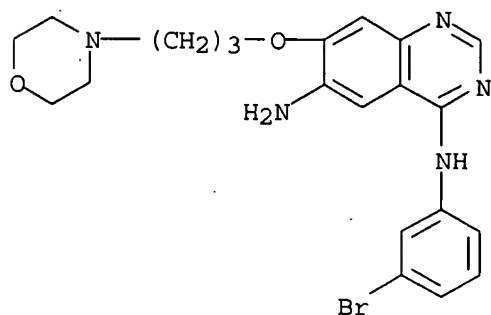
IT 198961-78-3P 267243-68-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of N-{4-(3-chloro-4-fluorophenylamino)-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl}acrylamide as an irreversible inhibitor of tyrosine kinases)

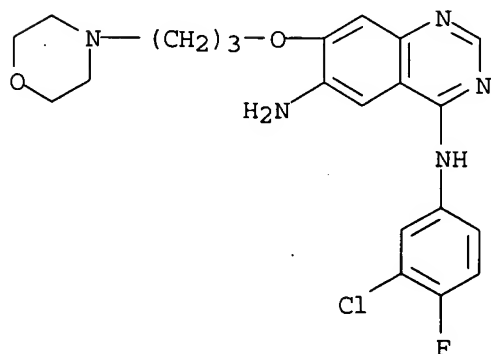
RN 198961-78-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



RN 267243-68-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



AB The title compd. that is an irreversible inhibitor of tyrosine kinases such as EGFR, erbB2, and erbB4, and inhibitor of the tyrosine phosphorylation of erbB3 and VEGF secretion (biol. data were given), was prepd. The title compd. is useful in treating cancer, restenosis, atherosclerosis, endometriosis, and psoriasis.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 2000:164843 CAPLUS

DN 132:317628

TI Tyrosine kinase inhibitors. 17. Irreversible inhibitors of the epidermal growth factor receptor: 4-(Phenylamino)quinazoline- and

4-(Phenylamino)pyrido[3,2-d]pyrimidine-6-acrylamides bearing additional solubilizing functions

AU Smaill, Jeff B.; Rewcastle, Gordon W.; Loo, Joseph A.; Greis, Kenneth D.; Chan, O. Helen; Reyner, Eric L.; Lipka, Elke; Showalter, H. D. Hollis; Vincent, Patrick W.; Elliott, William L.; Denny, William A.

CS Auckland Cancer Society Research Centre Faculty of Medical and Health Sciences, The University of Auckland, Auckland, N. Z.

SO Journal of Medicinal Chemistry (2000), 43(7), 1380-1397

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT 198961-78-3P 198961-84-1P 198961-86-3P

198961-87-4P 267243-67-4P 267243-68-5P

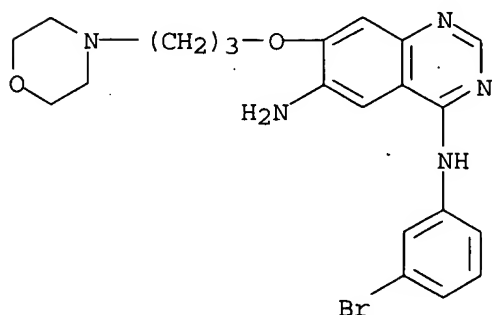
267243-69-6P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(antitumor and EGFR enzyme-inhibiting SAR of quinazolines)

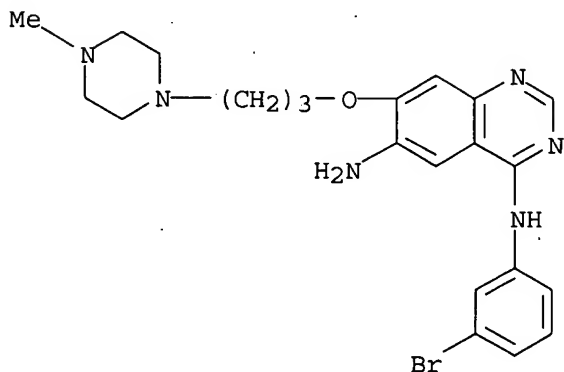
RN 198961-78-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



RN 198961-84-1 CAPLUS

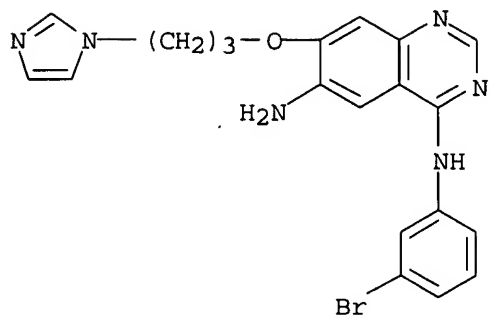
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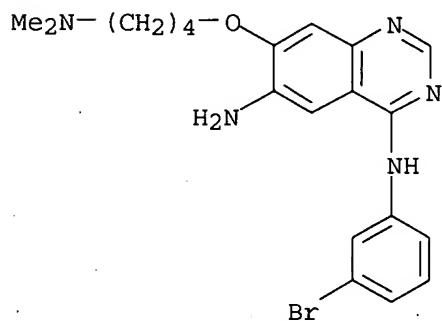
RN 198961-86-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy]-(9CI) (CA INDEX NAME)

(9CI) (CA INDEX NAME)

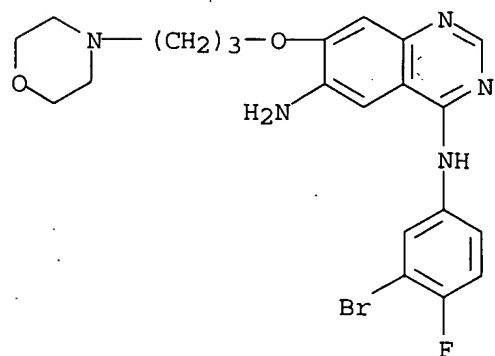


RN 198961-87-4 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy]-
(9CI) (CA INDEX NAME)

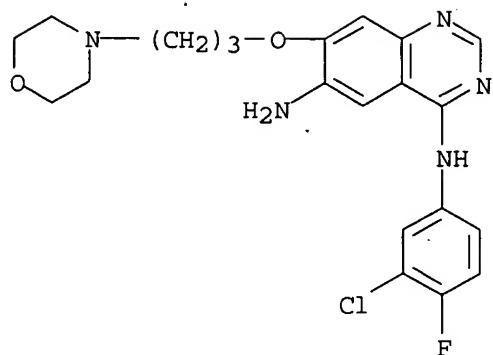
RN 267243-67-4 CAPLUS

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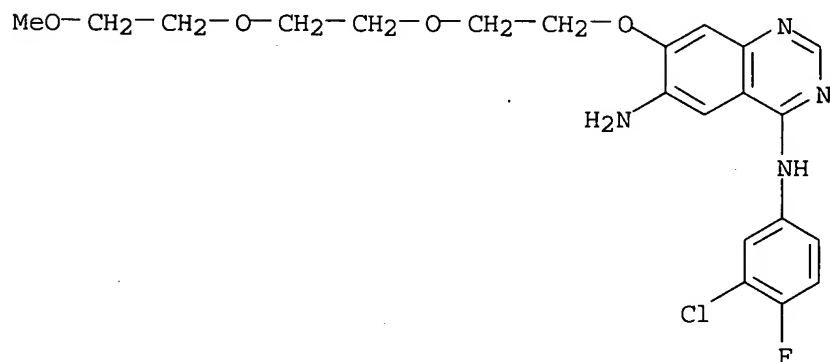
RN 267243-68-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 267243-69-6 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy]- (9CI) (CA INDEX NAME)

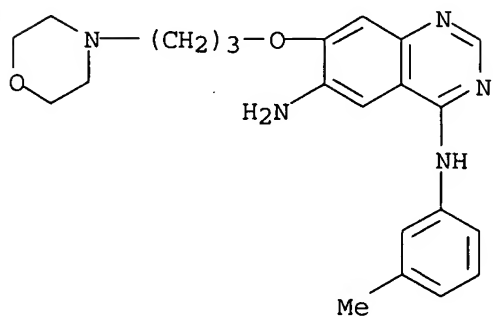


IT 198961-80-7P 198961-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines)

RN 198961-80-7 CAPLUS

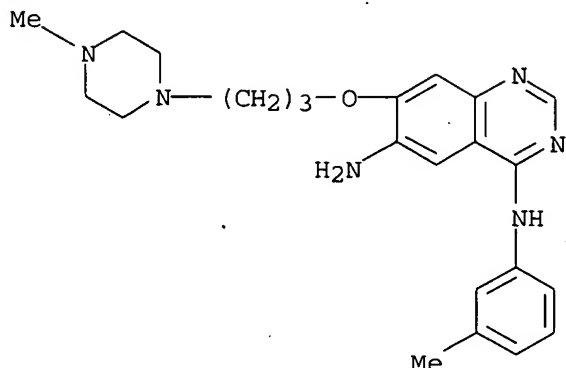
CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 198961-82-9 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-

piperazinyl)propoxy] - (9CI) (CA INDEX NAME)



AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,2-d]pyrimidine-6-acrylamides substituted with solubilizing 7-alkylamine or 7-alkoxyamine side chains were prepd. by reaction of the corresponding 6-amines with acrylic acid or acrylic acid anhydrides. In the pyrido[3,2-d]pyrimidine series, the intermediate 6-amino-7-alkylamines were prepd. from 7-bromo-6-fluoropyrido[3,2-d]pyrimidine via Stille coupling with the appropriate stannane under palladium(0) catalysis. This proved a versatile method for the introduction of cationic solubilizing side chains. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Quinazoline analogs with 7-alkoxyamine solubilizing groups were potent irreversible inhibitors of the isolated EGFR enzyme, with IC₅₀[app] values from 2 to 4 nM, and potentially inhibited both EGFR and erbB2 autophosphorylation in cells. 7-Alkylamino- and 7-alkoxyaminopyrido[3,2-d]pyrimidines were also irreversible inhibitors with equal or superior potency against the isolated enzyme but were less effective in the cellular autophosphorylation assays. Both quinazoline- and pyrido[3,2-d]pyrimidine-6-acrylamides bound at the ATP site alkylating cysteine 773, as shown by electrospray ionization mass spectrometry, and had similar rates of absorptive and secretory transport in Caco-2 cells. A comparison of two 7-propoxymorpholide analogs showed that the pyrido[3,2-d]pyrimidine-6-acrylamide had greater amide instability and higher acrylamide reactivity, being converted to glutathione adducts in cells more rapidly than the corresponding quinazoline. This difference may contribute to the obsd. lower cellular potency of the pyrido[3,2-d]pyrimidine-6-acrylamides. Selected compds. showed high in vivo activity against A431 xenografts on oral dosing, with the quinazolines being superior to the pyrido[3,2-d]pyrimidines. Overall, the quinazolines proved superior to previous analogs in terms of aq. soly., potency, and in vivo antitumor activity, and one example (CI 1033) has been selected for clin. evaluation.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

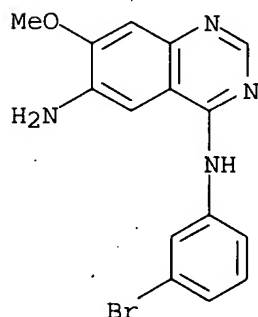
L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1998:323483 CAPLUS

DN 129:119500

TI Inhibitors of the epidermal growth factor receptor protein tyrosine kinase. A quantitative structure-activity relationship analysis

AU Singh, P.; Kumar, R.
CS Department Chemistry, S. K. Government College, Sikar, 332001, India
SO Journal of Enzyme Inhibition (1998), 13(2), 125-134
CODEN: ENINEG; ISSN: 8755-5093
PB Harwood Academic Publishers
DT Journal
LA English
IT 171745-06-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(quant. structure-activity relationship of inhibitors of the epidermal growth factor receptor protein tyrosine kinase)
RN 171745-06-5 CAPLUS
CN 4,6-Quinazolininediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB Hansch and Free-Wilson analyses are described on a data set, 4-anilinoquinazolines [the analogs of 4-(3-bromo-anilino)-6,7-dimethoxy quinazoline: PD 153035], as inhibitors of the epidermal growth factor receptor protein tyrosine kinase. These analyses have helped to ascertain the role of different substituents in explaining the obsd. inhibitory activities. From both approaches, it is concluded that the combined electron-donating nature of R1- and R2-substitutions of the quinazoline ring and the electron-withdrawing nature of the X-substitution of the anilino-ring are beneficial for increasing the inhibition activity of a compd. Further, the sym. alkoxy substituents present at the R1- and R2-positions are also engaged in a steric interaction which was detd. quant. through the parabolic relationship between the activity and combined molar refraction parameter, .SIGMA.MR of the substituents.

L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1997:696745 CAPLUS
DN 128:3695
TI Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors
IN Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.
PA Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong
SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738983	A1	19971023	WO 1997-US5778	19970408
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	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	AU 725533	B2	20001012		
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
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	CN 1218456	A	19990602	CN 1997-194458	19970408
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				WO 1997-US5778 W	19970408
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	JP 3370340	B2	20030127		
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				WO 1997-US5778 W	19970408
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				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	ES 2174250	T3	20021101	ES 1997-920213	19970408
				US 1996-15351P P	19960412
	ZA 9703060	A	19971104	ZA 1997-3060	19970410
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	BG 63160	B1	20010531	BG 1998-102811	19981001
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
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				WO 1997-US5778 W	19970408
	KR 2000005364	A	20000125	KR 1998-708086	19981010
				US 1996-15351P P	19960412
	US 6344459	B1	20020205	US 1999-155501	19990608
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408

OS MARPAT 128:3695

IT 198961-78-3P 198961-80-7P 198961-82-9P

198961-84-1P 198961-86-3P 198961-87-4P

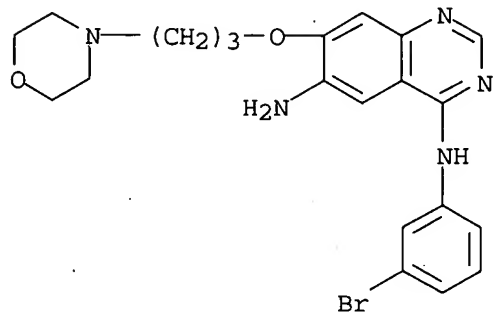
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase

inhibitors)

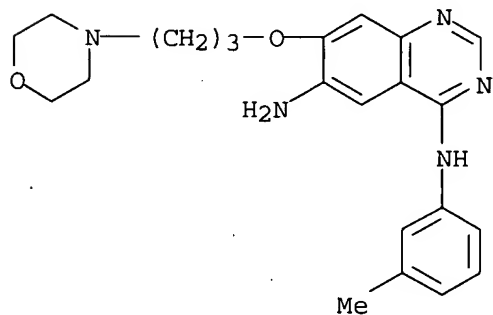
RN 198961-78-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



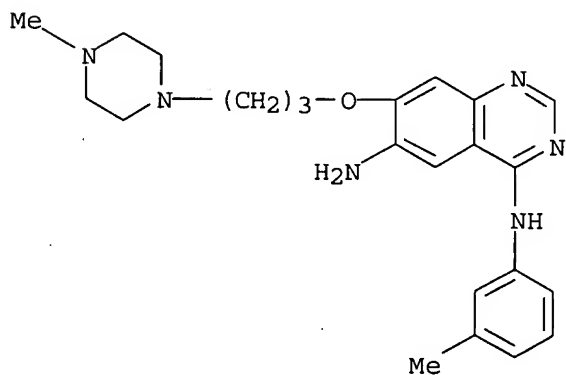
RN 198961-80-7 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



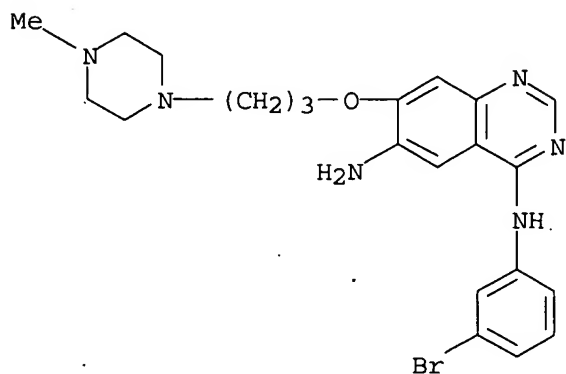
RN 198961-82-9 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]-(9CI) (CA INDEX NAME)



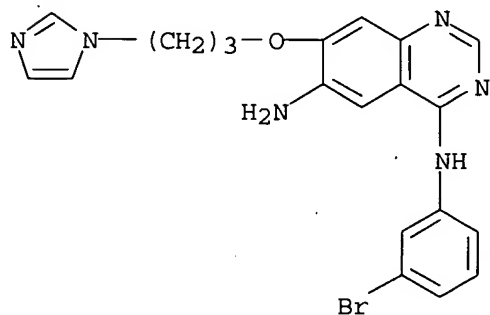
RN 198961-84-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]-(9CI) (CA INDEX NAME)



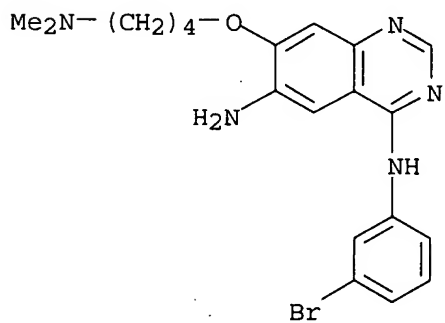
RN 198961-86-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy]-(9CI) (CA INDEX NAME)

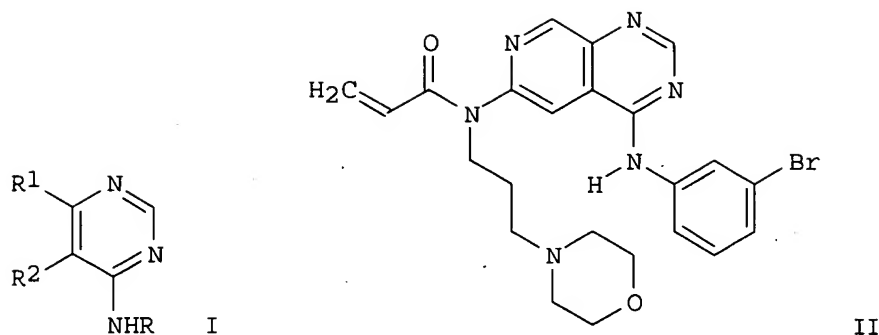


RN 198961-87-4 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy]-(9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1Z2R10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinopropylamine and the product acylated by CH2:CHCOCl to give title compd. II. Data for biol. activity of I were given.

L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1996:756470 CAPLUS

DN 126:18889

TI Preparation of 6-(2-methoxyethylamino)-7-methoxy-4-(3'-methylanilino)quinazoline cell proliferation inhibitor

IN Barker, Andrew John

PA Zeneca Limited, UK

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9633981	A1	19961031	WO 1996-GB962	19960423
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	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN			
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	AU 9653434	A1	19961118	AU 1996-53434	19960423
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				WO 1996-GB962	W 19960423
	EP 823901	A1	19980218	EP 1996-910135	19960423
	EP 823901	B1	20001018		
	R:	CH, DE, FR, GB, IT, LI			
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				WO 1996-GB962	W 19960423
	JP 11504034	T2	19990406	JP 1996-532253	19960423

US 5952333 A 19990914

GB 1995-8535 A 19950427
 WO 1996-GB962 W 19960423
 US 1997-930044 19970926
 GB 1995-8535 A 19950427
 WO 1996-GB962 W 19960423

OS MARPAT 126:18889

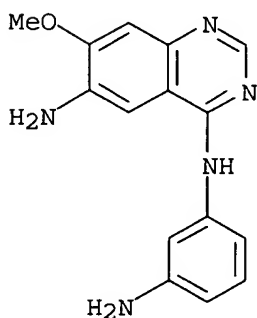
IT 184473-34-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(prepn. of 6-(2-methoxyethylamino)-7-methoxy-4-(3'-
 methylanilino)quinazoline cell proliferation inhibitor)

RN 184473-34-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-aminophenyl)-7-methoxy- (9CI) (CA INDEX
 NAME)



AB 6-(2-Methoxyethylamino)-7-methoxy-4-(3'-methylanilino)quinazoline, useful
 as a cell-inhibiting tyrosine kinase receptor inhibitor for the treatment
 of proliferative diseases such as cancer (no data), prepd. by the reaction
 of 2-methoxyacetaldehyde di-Me acetal and 6-amino-7-methoxy-4-
 (3'-methylanilino)quinazoline in the presence of NaBH4, demonstrated a IC50
 of 0.01 .mu.M against the enzyme EGF receptor tyrosine kinase.

L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1996:483485 CAPLUS

DN 125:142741

TI Prepn. of N-phenyl-4-quinazolinamines for the treatment of proliferative
 diseases

IN Brown, Dearg Sutherland; Morris, Jeffrey James; Thomas, Andrew Peter

PA Zeneca Limited, UK

SO PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615118	A1	19960523	WO 1995-GB2606	19951108
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

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CA 2200871	AA	19960523	CA 1995-2200871	19951108
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AU 9538130	A1	19960606	AU 1995-38130	19951108
AU 703328	B2	19990325		
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EP 790986	A1	19970827	EP 1995-936044	19951108
EP 790986	B1	19990120		
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AT 175962	E	19990215	AT 1995-936044	19951108
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ES 2128092	T3	19990501	ES 1995-936044	19951108
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ZA 9509572	A	19960513	ZA 1995-9572	19951110
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FI 9701970	A	19970507	FI 1997-1970	19970507
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
NO 9702152	A	19970512	NO 1997-2152	19970509
			GB 1994-22866	19941112
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			WO 1995-GB2606	19951108
US 5821246	A	19981013	US 1997-836362	19970521
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			GB 1995-7308	19950407
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OS MARPAT 125:142741

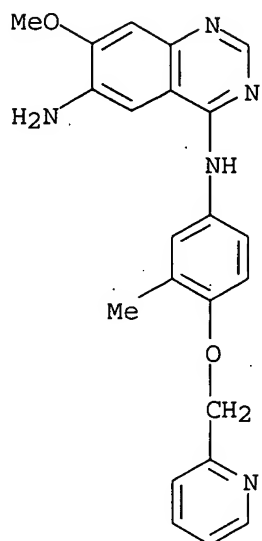
IT **179688-72-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

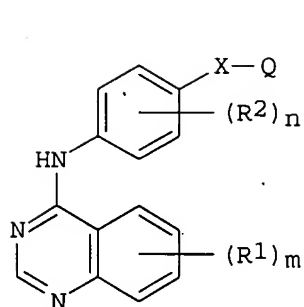
(prepn. of N-phenylquinazolinamines as tyrosine kinase inhibitors)

RN 179688-72-3 CAPLUS

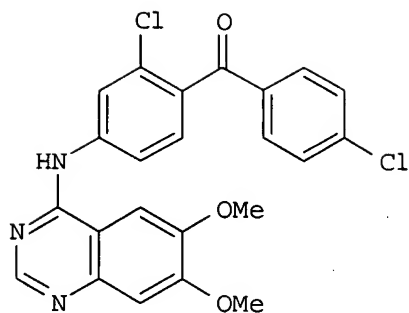
CN 4,6-Quinazolinediamine, 7-methoxy-N4-[3-methyl-4-(2-pyridinylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



GI



I



II

AB The title compds. I ($m = 1-3$; $R_1 =$ halo, hydroxy, amino, ureido, etc.; $n = 0-3$; $R_2 =$ halo, trifluoromethyl, hydroxy, amino, nitro, cyano, alkyl; $X =$ carbonyl, methine, O,S, etc.) were disclosed. I were claimed for the use as receptor tyrosine kinase inhibitors and for treatment of proliferative disease such as cancer. An example compd. is the chlorophenyl [(quinazolinyl)amino]phenyl methanone II.

L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1996:476843 CAPLUS

DN 125:142761

TI Quinazoline derivatives

IN Barker, Andrew John

PA Zeneca Limited, UK

SO PCT Int. Appl., 45 pp.

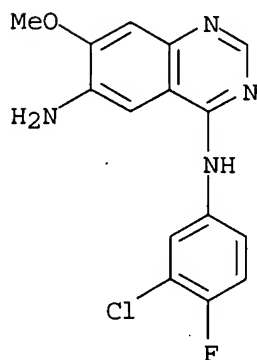
CODEN: PIXXD2

DT Patent

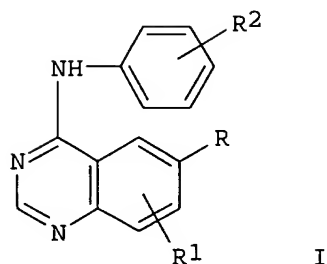
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616960	A1	19960606	WO 1995-GB2768	19951128
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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				GB 1994-24233	19941130
	US 5955464	A	19990921	US 1997-860088	19970522
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OS	MARPAT 125:142761				
IT	179552-75-1P				
	RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)				
	(prepn. of tyrosine kinase inhibiting imidazolylquinazolines)				
RN	179552-75-1 CAPLUS				
CN	4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-methoxy- (9CI) (CA INDEX NAME)				



GI



AB The invention concerns quinazoline derivs. I (m = 1, 2; R1 = H, halo, alkyl, alkoxy; n = 1-3; R2 = H, OH, halo, alkyl; R = 5- or 9-membered nitrogen-linked heteroaryl moiety contg. up to four nitrogen heteroatoms, or R = a 5-, 6-, 9- or 10-membered nitrogen-linked unsatd. heterocyclic moiety contg. up to three nitrogen heteroatoms which bears one or two substituents selected from oxo and thioxo) and the use of the receptor tyrosine kinase inhibitory properties of the compds. in the treatment of proliferative diseases such as cancer. Among the approx. 15 title compds. prepd., 4-(3-methylanilino)-, 4-(3-chloro-4-fluoroanilino)-, 4-(4-benzoyl-3-chloroanilino)-, and 4-[3-methyl-4-(2-pyridylmethoxy)anilino]-6-(1-imidazolyl)quinazolines were claimed.

L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1996:312235 CAPLUS

DN 125:25623

TI Structure-activity relationships for 4-anilinoquinazolines as potent inhibitors at the ATP binding site of the epidermal growth factor receptor in vitro

AU Denny, William A.; Rewcastle, Gordon W.; Bridges, Alexander J.; Fry, David W.; Kraker, Alan J.

CS Cancer Research Lab., Univ. Auckland School Medicine, Auckland, 92019, N. Z.

SO Clinical and Experimental Pharmacology and Physiology (1996), 23(5), 424-427

CODEN: CEXPB9; ISSN: 0305-1870

PB Blackwell

DT Journal

LA English

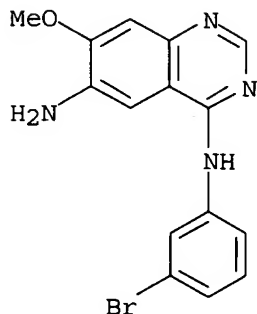
IT 171745-06-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anilinoquinazolines as potent inhibitors at ATP binding site of epidermal growth factor receptor)

RN 171745-06-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB Structure-activity relationships are described for the inhibition of the tyrosine kinase activity (phosphorylation of a fragment of phospholipase Cg1) of the epidermal growth factor receptor (EGFR) by 4-anilinoquinazolines. These compds. are competitive inhibitors at the ATP binding site. The preferred side chain is anilino-, substituted at the 3-position with small lipophilic groups. The quinazoline moiety is absolutely required for activity, but substituents on the quinazoline greatly modulate potency, with electron-donating groups favored. The most potent analog, the 6,7-dimethoxy deriv., has an IC₅₀ of 29 pmol/L and a very high selectivity for the EGFR over other tyrosine kinase enzymes. The present study shows that it is possible to identify small mols. that are very potent, yet highly selective, inhibitors of a single component of the growth signal transduction pathway in cells.

L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1995:983167 CAPLUS

DN 124:21051

TI Tyrosine kinase inhibitors: unusually steep structure-activity relationship for analogs of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline (PD 153035), a potent inhibitor of the epidermal growth factor receptor

AU Bridges, Alexander J.; Zhou, Hairong; Cody, Donna R.; Rewcastle, Gordon W.; McMichael, Amy; Showalter, H. D. Hollis; Fry, David W.; Kraker, Alan J.; Denny, William A.

CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48106-1047, USA

SO Journal of Medicinal Chemistry (1996), 39(1), 267-76

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT 171745-06-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

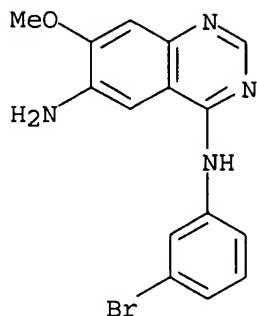
(epidermal growth factor receptor tyrosine kinase inhibitors:

structure-activity relations for analogs of

(bromoanilino)dimethoxyquinazoline (PD 153035))

RN 171745-06-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB 4-(3-Bromoanilino)-6,7-dimethoxyquinazoline (PD 153035) is a very potent inhibitor (IC₅₀ 0.025 nM) of the tyrosine kinase activity of the EGF receptor, binding competitively at the ATP site. Structure-activity relations for close analogs of PD 153035 are very steep. Some derivs. have IC₅₀ .1 to req. 80-fold better than predicted from simple additive binding energies, yet analogs possessing combinations of similar Ph and quinazoline substituents do not show this supra-additive effect. Some substituents which are mildly deactivating by themselves can be strongly activating when used in the correct combinations; therefore, certain substituted analogs may induce a change in conformation of the receptor when they bind. There is some bulk tolerance for substitution in the 6- and 7-positions of the quinazoline, so that PD 153035 is not the optimal inhibitor for the induced conformation. 4-(3-Bromoanilino)-6,7-diethoxyquinazoline shows an IC₅₀ of 0.006 nM, making it the most potent inhibitor of the tyrosine kinase activity of the EGF receptor yet reported.

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS
 AN 1994:217715 CAPLUS
 DN 120:217715
 TI Quinazoline tyrosine kinase-inhibiting anticancer agents
 IN Barker, Andrew J.
 PA Zeneca Ltd., UK
 SO Can. Pat. Appl., 99 pp.
 CODEN: CPXXEB
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2086968	AA	19930721	CA 1993-2086968	19930108
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	ZA 9300015	A	19930720	ZA 1993-15	19930104
				GB 1992-1095	A 19920120
	AU 9331010	A1	19930722	AU 1993-31010	19930104
	AU 661533	B2	19950727		
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				GB 1992-13572	A 19920626
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	HU 63153	A2	19930728	HU 1993-94	19930115
				GB 1992-1095	A 19920120
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OS MARPAT 120:217715

IT **153437-12-8P**

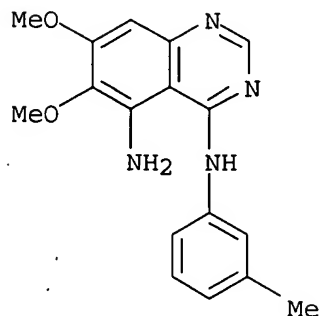
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of, as intermediate in prepn. of quinazoline tyrosine .kinase-inhibiting anticancer agents)

RN 153437-12-8 CAPLUS

CN 4,5-Quinazolinediamine, 6,7-dimethoxy-N4-(3-methylphenyl)- (9CI) (CA

INDEX NAME)



IT 153437-18-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of, as tyrosine kinase-inhibiting anticancer agent)

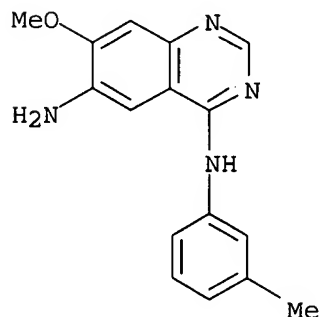
RN 153437-18-4 CAPLUS

CN 4,6-Quinazolinediamine, 7-methoxy-N4-(3-methylphenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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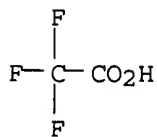
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 153437-17-3P

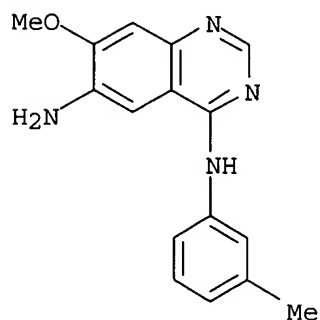
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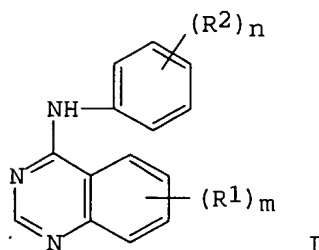
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(tyrosine kinase-inhibiting anticancer agent)

RN 153437-17-3 CAPLUS

CN 4,6-Quinazolinediamine, 7-methoxy-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



GI



I

AB The title compds. I [R1 = HO, (un)substituted amino, carboxy, carbamoyl, ureido, etc.; R2 = H, HO, halogen, CF3, NH2, NO2, CN, (un)substituted C1-4 alkyl, etc.; m = 1-3; n = 1, 2], useful as tyrosine kinase-inhibiting anticancer agents (no data), are prepd. and I-contg. formulations presented. Thus, 4-chloro-6,7-dimethoxyquinazoline was condensed with 3-MeC6H4NH2, producing 6,7-dimethoxy-4-(3'-methylanilino)quinazoline hydrochloride, m.p. 248-249.degree..

=> s l4 and Tyrosine kinase
L5 18 L4 AND TYROSINE KINASE

=> d his

(FILE 'HOME' ENTERED AT 14:38:38 ON 01 JUL 2003)

FILE 'REGISTRY' ENTERED AT 14:38:47 ON 01 JUL 2003

L1 STRUCTURE UPLOADED

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L3 82 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:39:27 ON 01 JUL 2003

L4 24 S L3

Patel

<7/1/2003>

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L5 18 S L4 AND TYROSINE KINASE

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